

**Ene Addition Reactions Involving  
Jojoba Bean Oil,  
Triglyceride Vegetable Oils and  
Synthetic Lubricant Fluids**

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Mass Spectroscopy in Action - 5 Lectures

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## **Papers Published**

Ene reactions of jojoba oil with 4-phenyl-1,2,4-triazoline-3,5-dione and diethyl azodicarboxylate.

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Hydroxymethylation of jojoba oil by Lewis acid-catalysed ene reaction with formaldehyde.

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## Abstract

Ene addition reactions involving jojoba bean oil (a wax ester), sunflower oil (a triglyceride) and the synthetic fluids polyisobutene and polyalphaolefin have been investigated. Several enophiles have been employed, including azo compounds [diethyl azodicarboxylate (DEAD), 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD) and 4-methyl-1,2,4-triazoline-3,5-dione (MTAD)], a sulfinyl compound [*N*-sulfinyl-*p*-toluenesulfonamide (TosNSO)] and formaldehyde.

In order to investigate the scope of these reactions, and to gain spectral information for use in the analysis of more complex product mixtures, model alkenes were studied. For this purpose, methyl oleate, methyl elaidate and oleyl acetate were chosen, as were the symmetrical simple alkenes 3-hexene and 5-decene, and a series of terminal alkenes. In each case, identification and characterisation of addition products was achieved principally by NMR ( $^1\text{H}$  and  $^{13}\text{C}$ ) and FAB mass spectroscopy.

Addition of the azo enophiles to jojoba oil and the mono-ene models resulted, in most cases, in the formation of adducts containing an alkene double bond with exclusively *trans* configuration. The exception to this was the addition of DEAD to 1-alkenes which resulted in adducts with *ca.* 20% of *cis* units. Where the lipid ene components were unsymmetrically substituted, the products were formed as 1:1 mixtures of regioisomers, as determined by high field  $^{13}\text{C}$  NMR spectroscopy. Kinetic measurements were made on the relative reactivities towards PTAD of methyl oleate, methyl elaidate, jojoba and *trans*-jojoba by two methods: using UV-visible spectroscopy to follow the consumption of the enophiles and secondly, by monitoring the relative rates of disappearance of the lipid components by capillary gas chromatography. These measurements confirmed the visual observation that *cis* ene components reacted more quickly with PTAD than those with *trans* geometry.

On reaction of the azo compounds with methyl linoleate, three major adduct types were isolated: non-conjugated dienes, conjugated dienes and diadducts resulting from a tandem ene/Diel-Alder cycloaddition sequence. The ratio of these three adduct types was found to vary depending on the enophile. With the triazolines the non-conjugated dienes and tandem diadducts predominated while, conversely, for DEAD the conjugated dienes were the major products. In order to determine the stereochemistry of the tandem diadducts, further model studies were carried out on 1,4-pentadiene and 2,4-*cis,trans*-hexadiene. An X-ray crystal structure of the hexadiene-PTAD adduct was obtained and used to confirm the more complex methyl linoleate diadduct geometries. The results of these model studies were useful in the assignment of the complex product mixtures formed during ene modifications of vegetable oils.

*N*-Sulfinyl-*p*-toluenesulfonamide additions to jojoba were carried out after preliminary model reactions on *cis*-5-decene and methyl oleate had been investigated. Diastereomeric adduct pairs were formed as a result of the asymmetric nature of the sulfur atom in the adducts.

Ethylaluminium dichloride catalysed additions of formaldehyde have been investigated. Reaction with both double bonds in jojoba furnished dihydroxymethyl jojoba, which was further modified by esterification of the hydroxy substituents to yield the benzoyl ester. Products were identified by comparison with adducts formed from oleyl acetate and methyl oleate. Hydrogenation of the alkene units ( $H_2/Pd-C$ ) was also carried out. On addition of formaldehyde to methyl linoleate, non-conjugated diene type adducts predominated. There was no evidence for tandem ene/Diels-Alder diadduct formation and only a trace of the conjugated diene adduct was observed.

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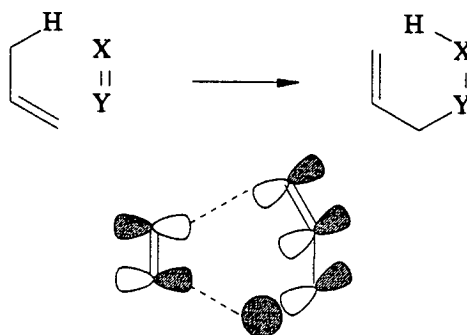
# **1. INTRODUCTION**

## **1.1 Foreword**

This thesis is concerned with the modification of vegetable oils *via* the ene reaction. The ene reaction bears similarities to the Diels-Alder cycloaddition and offers wide synthetic scope, however it is often neglected in undergraduate textbooks. An overview of the reaction follows, with emphasis on features relevant to this work. Subsequent chapters are devoted to the two types of vegetable oil which have been studied. Firstly, the liquid wax ester derived from the jojoba plant and secondly, the more typical triglycerides which are found in most seed oils. The synthetic polyalphaolefins and polyisobutenes (which are used in the lubricants industry) have also been investigated and their ene additions will be discussed.

## 1.2 The Ene Reaction

Since Alder originally defined the Ene Reaction in 1943,<sup>1</sup> there have been numerous articles published on the subject.<sup>2-6</sup> In his comprehensive review of 1969,<sup>7</sup> Hoffmann described the reaction as the addition of a compound containing a double bond to an olefin possessing an allylic hydrogen (ene), involving allylic shift of a double bond, transfer of the allylic hydrogen to the enophile and bonding between the two unsaturated termini (Scheme 1).

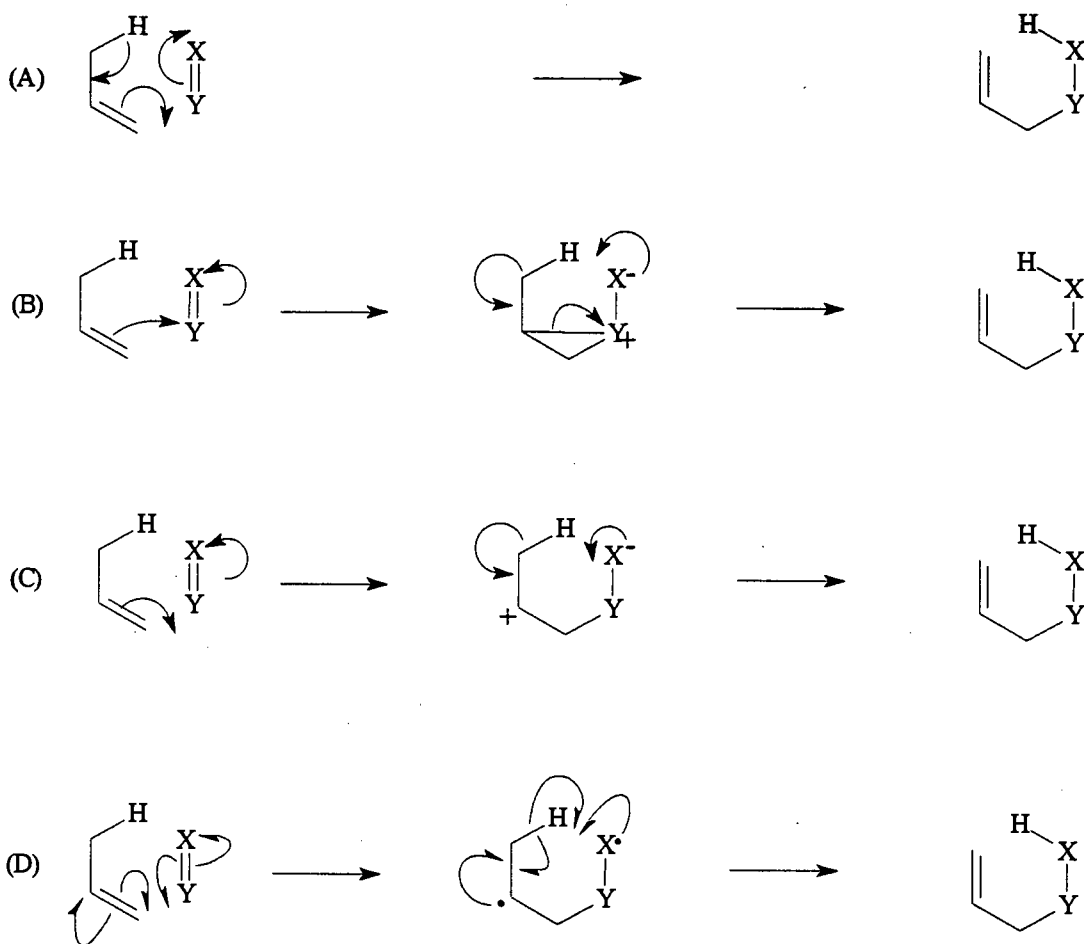


Scheme 1

The reaction resembles the Diels-Alder cycloaddition with two of the diene  $\pi$ -electrons replaced by the two electrons of the allylic C-H  $\sigma$ -bond. The ene addition generally has a greater activation energy and consequently requires higher temperatures. Using frontier molecular orbital (FMO) theory, the mode of addition has been described<sup>8</sup> as a suprafacial three-component interaction among the HOMO of the ene, the LUMO of the allylic C-H bond, and the LUMO of the enophile (Scheme 1). The Woodward-Hoffmann orbital symmetry rules describe the  $[2\sigma+2\pi+2\pi]$  concerted reaction as allowed. The reaction has been the subject of theoretical calculations; for example, Paderes and Jorgensen<sup>9</sup> have recently modified the computer programme CAMEO (which utilises FMO theory) to predict the feasibility and regiochemistry of the ene reaction.

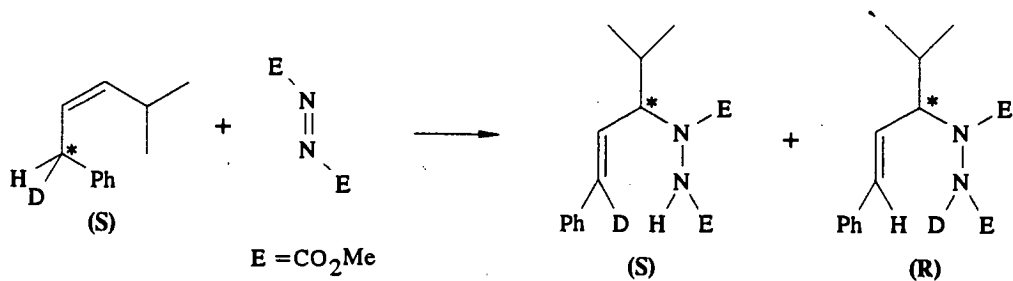
There has been much debate about the mechanism of the ene reaction and no single pathway appears to be able to explain all its features - even with one

particular enophile.<sup>10</sup> The main models which have been proposed are shown in Scheme 2. These can be categorised into concerted (A) or stepwise (B, C and D) *via* an intermediate, zwitterion or diradical.



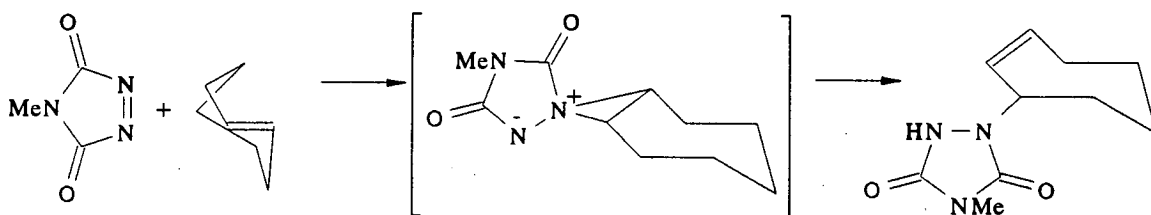
Scheme 2

There is experimental evidence for a concerted process<sup>11</sup> (mechanism A) in the reaction of dimethyl azodicarboxylate with (S)-*cis*-1-deuterio-4-methyl-1-phenylpentene (Scheme 3). For a suprafacial-suprafacial pathway, attack from above the plane gives the R stereoisomer while attack from below gives the S. A kinetic isotope effect of 3.3 was found for the abstraction of H vs. D from the benzylic chiral centre. As this coincided with the ratio of the two enantiomers formed by the C-N bond creation (S/R = 3.1), the reaction was deemed to be fully in accord with a concerted mechanism.



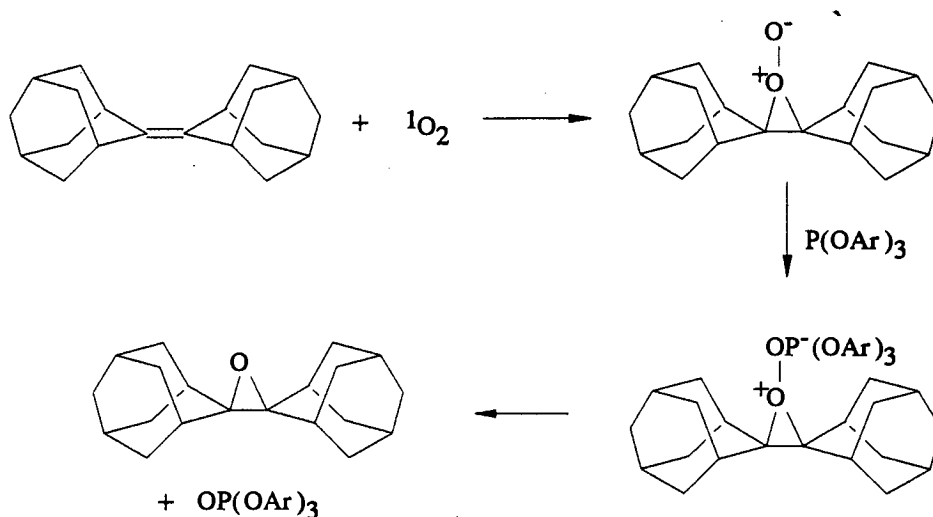
**Scheme 3**

In contrast, although calculations indicate that the concerted (mechanism A) and one of the stepwise pathways (mechanism B) have similar energy requirements (for the reaction of propene with a variety of enophiles),<sup>12</sup> the latter has been favoured for triazolidiones and singlet oxygen.<sup>13,14,15</sup> An aziridinium imide intermediate has been characterised spectroscopically at  $-135^\circ\text{C}$  in the reaction of 4-methyl-1,2,4-triazoline-3,5-dione (MTAD) with *trans*-cycloheptene (Scheme 4).



**Scheme 4**

Aziridinium imides have also been trapped with methanol.<sup>17</sup> On addition of 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD) to *cis* and *trans*-2-butenes, different stereospecific methanol adducts were formed. This gives further evidence for a structurally rigid intermediate in the ene reaction rather than an open zwitterionic intermediate (which could undergo rotational equilibration). Similarly, with  $^1\text{O}_2$  as enophile, a perepoxide has been trapped (which subsequently formed an epoxide) in the reaction with adamantylideneadamantane in the presence of a phosphite<sup>18</sup> (Scheme 5).



**Scheme 5**

The diradical and zwitterionic mechanisms (D & C) are usually rejected because of the lack of evidence of rearrangements which are characteristic of carbon radicals and carbocations.

A variety of factors which may influence the course of the ene reaction have been investigated including solvent polarities,<sup>14,19</sup> rotational barriers,<sup>20</sup> steric<sup>21</sup> and electrostatic<sup>22</sup> effects and quantum mechanical tunnelling.<sup>23</sup> These observations provide further support for a stepwise mechanism (type B in Scheme 2) for triazolines and singlet oxygen as enophiles.

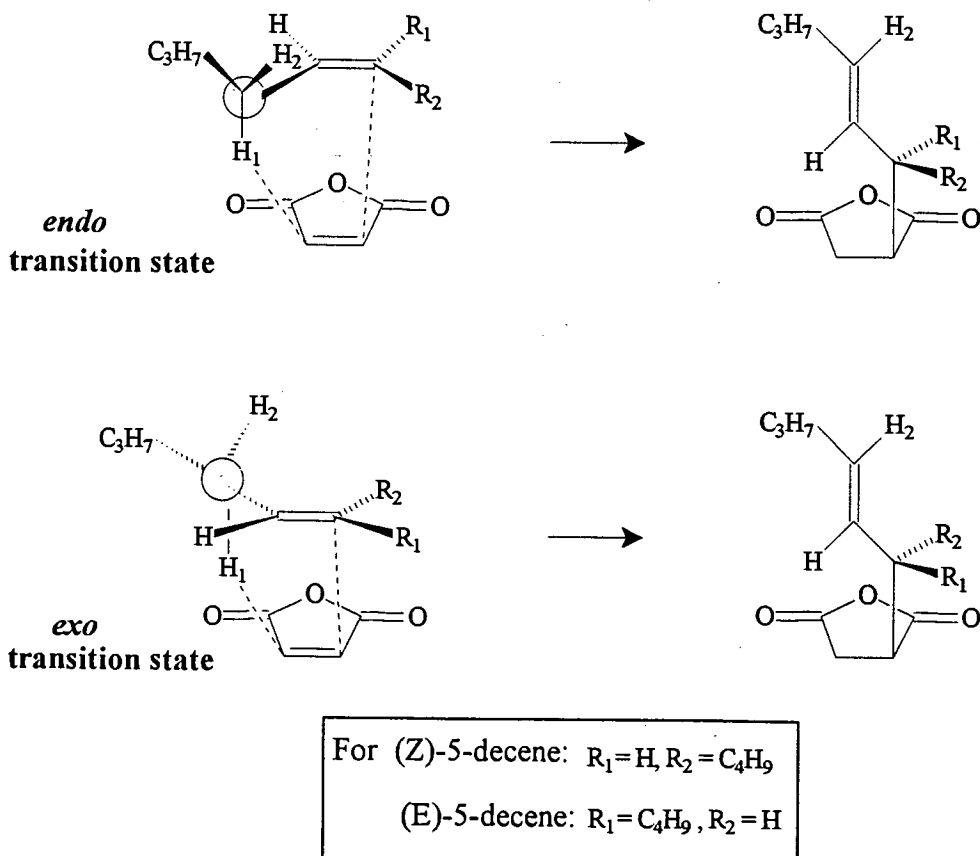
The subsequent sections detail the scope of the ene reaction by describing the types of enophiles and ene components that this addition encompasses.

### 1.3 The Enophile Component:

The variety of enophiles makes the ene reaction very versatile from a synthetic point of view; reactive components which have been used include:

#### 1.3.1 Alkenes and Alkynes

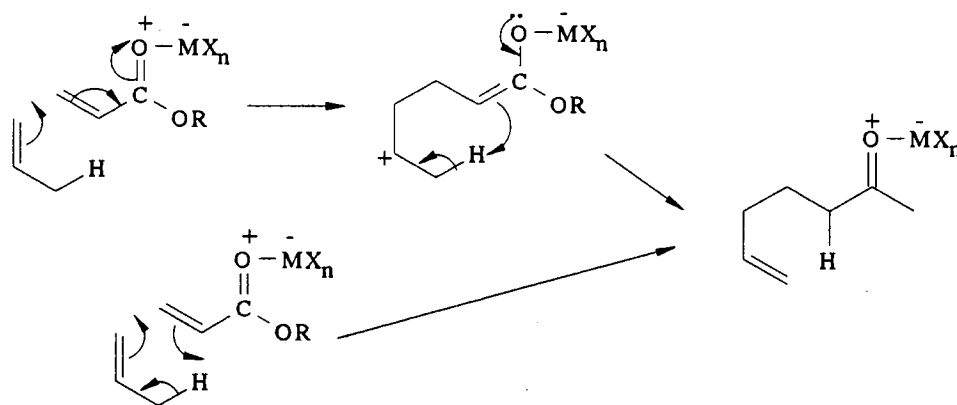
Simple alkenes do not function as enophiles, but require electron withdrawing groups to activate them; for example, maleic anhydride, methyl acrylate and acrylonitrile. Even with activating substituents, these reactions still require high temperatures (*ca.* 200°C) and prolonged heating. Maleic anhydride in its reaction with unsaturated fatty acids and esters represents the first recorded examples of ene reactions in all carbon systems.<sup>7</sup> Nahm and Cheng<sup>24</sup> have further studied maleic anhydride as an enophile in its additions to a series of decenes. They found that there was a preference for the *endo* transition state with both *cis* and *trans* alkenes.



Scheme 6

Scheme 6 illustrates the *endo* and *exo* transition states using the 5-decenes as an example. The *endo:exo* ratios were found to be >8:1 for the *cis* alkene and 1.1:1 for the *trans*. The poorer selectivity for the *trans* alkene ( $R_1 = \text{Bu}$ ,  $R_2 = \text{H}$ ) was attributed to a repulsion between the butyl chain substituent and a carbonyl group in the *endo* transition state; this interaction is avoided in the *cis* case. The product geometries were exclusively *trans* in the former case and 82% *trans* in the latter. Formation of the *cis* product can be envisaged to involve abstraction of  $\text{H}_2$  in place of  $\text{H}_1$  (Scheme 6).

In the case of  $\alpha,\beta$ -unsaturated esters the enophilic activity can be greatly increased by catalysis. Lewis acids complex to the oxygen and effectively withdraw electrons from the alkene unit (Scheme 7),<sup>25</sup> thus accelerating the reaction in the same way as electron withdrawing substituents by lowering the LUMO of the enophile. The mechanism can be regarded as either concerted or stepwise.



Scheme 7

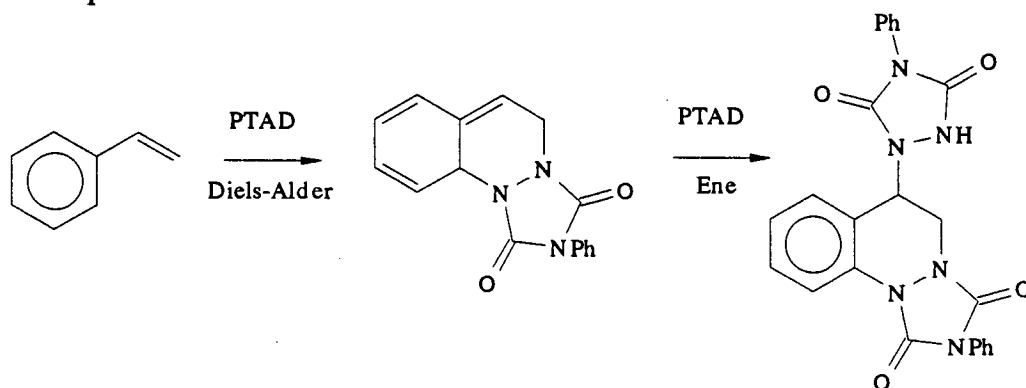
The most reactive alkene enophile known is 2,2-bis(trifluoromethyl)ethylene-1,1-dicarbonitrile  $[(\text{CF}_3)_2\text{C}=\text{C}(\text{CN})_2]$ <sup>26</sup> which even undergoes ene reactions with unactivated alkenes at room temperature.

In general, alkynes undergo the ene reaction more readily than the corresponding alkenes. Benzyne is a highly reactive<sup>7</sup> triply-bonded species, while dicyanoacetylene and hexafluoro-2-butyne have also been used.



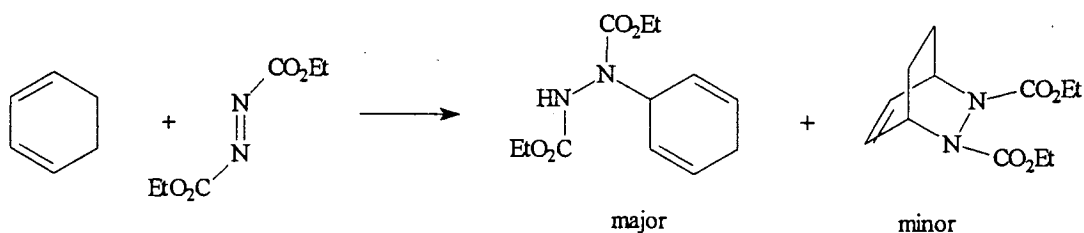
### 1.3.2 Azo compounds

These far surpass the above carbon systems in reactivity. 4-Phenyl-1,2,4-triazoline-3,5-dione (PTAD), a "superenophile",<sup>27</sup> reacts readily and has been used to modify a variety of unsaturated systems including polydienes.<sup>28</sup> Corey & Snider<sup>29</sup> used it in a key hydrazine forming step during a prostaglandin synthesis, and its dienophilic properties were utilised in its reaction with styrene<sup>30</sup> (Scheme 8) where ene addition occurred to the initial Diels-Alder addition product.



Scheme 8

Indeed, Diels-Alder additions, ene reactions and [2+2] cycloadditions can often compete with each other, depending on the geometry and functionalisation of the ene and (di)enophile components; *eg.* in the reaction of 1,3-cyclohexadiene with diethyl azodicarboxylate (DEAD) both ene and Diels-Alder adducts are formed with the ene adduct predominating (8:1) (Scheme 9).<sup>31</sup>



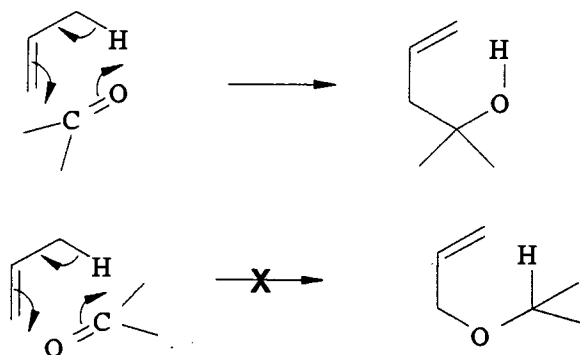
Scheme 9

A study of the kinetics and substituent effects in the reactions of triazolinediones with simple alkenes has been reported.<sup>32</sup> Substitution at the double bond was found to increase the alkene reactivity, *eg.* 1-alkenes were 10-20 times less reactive than 1,2-disubstituted alkenes, while the authors found that the reactivity of 2,3-dimethyl-2-butene was too great to be measured.

There has been a recent report on the use of Lewis acid catalysts to accelerate the addition of DEAD to simple alkenes.<sup>33</sup> The use of  $\text{SnCl}_4$  allowed additions to take place at  $-60^\circ\text{C}$  in five seconds compared with several hours at  $80-100^\circ\text{C}$  for the thermal reaction.

### 1.3.3 Carbonyl compounds

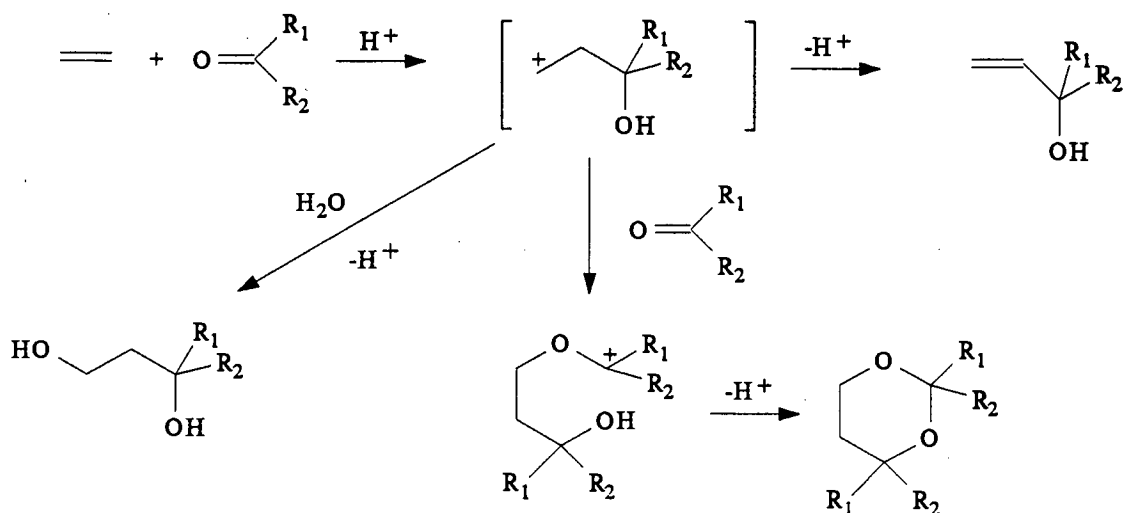
These could, conceivably, react with alkenes to form either homoallylic alcohols or allyl ethers (Scheme 10). However, consistent with the greater gain of bond energy, the alcohol is formed exclusively.



Scheme 10

The reaction of carbonyl compounds as enophiles is related to the Prins reaction, which is the acid catalysed addition of aldehydes to alkenes<sup>34</sup> and which is thought to proceed *via* electrophilic addition of a protonated aldehyde to the alkene (Scheme 11). This results in complex product mixtures as the

resulting carbocation may react further with any species present; *eg.* with water to give a 1,3-diol, with excess aldehyde to give a 1,3-dioxane, or with loss of a proton to form an allylic alcohol.



Scheme 11

As with the all carbon system, only carbonyl compounds activated by electron withdrawing groups are suitable; simple aldehydes and ketones do not react thermally. However, electron poor analogues such as trichloroacetaldehyde, ethyl glyoxylate and diethyl nitromalonate react at 120-200°C.<sup>2</sup> Carbonyl cyanide [CO(CN)<sub>2</sub>] has been used as an enophile and reacts with electron rich ene components such as *p*-methoxy and *p*-dimethylaminostyrene, but not with the electron withdrawing *p*-nitro substituted analogue.<sup>35</sup> Halogen substituted ketones such as hexafluoroacetone<sup>36</sup> and perfluorocyclobutanone<sup>37</sup> have also been used.

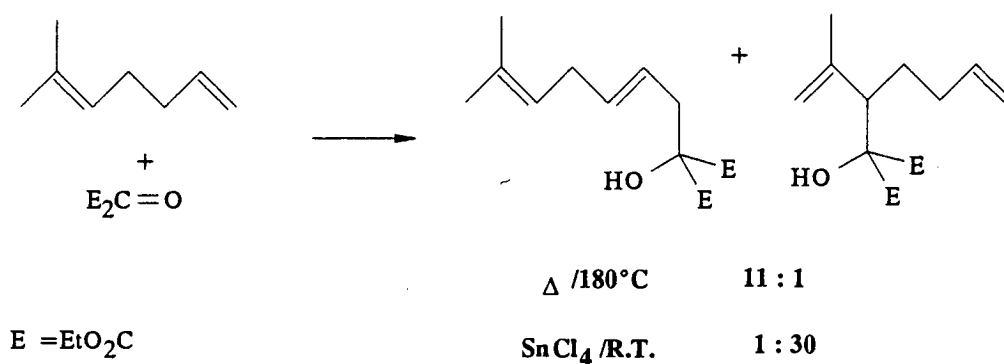
Extensive use has been made of Lewis acid catalysis to activate carbonyl compounds. These act by withdrawing electrons and thereby lowering the LUMO of the enophile, as described previously for the case of  $\alpha,\beta$ -unsaturated ester enophiles (Section 1.3.1). Snider *et al*<sup>25,38</sup> have made comprehensive studies on alkylaluminium halides and found them to be

particularly useful Lewis acid catalysts as they also act as proton scavengers, thus preventing unwanted proton-catalysed side reactions. The use of ethylaluminium dichloride<sup>39</sup> and dimethylaluminium chloride<sup>40</sup> with aldehydes has been investigated and some relevant points are summarised below.

Dimethylaluminium chloride gives moderate to good yields in the reactions of alkyl and aryl substituted aldehydes with alkenes. However, problems are encountered with tri- and tetra- substituted double bonds as methyl addition to the aldehyde can lead to alcohol side products, limiting the scope of the reaction. Also, alkenes which would give a secondary carbocation (see Scheme 7) do not react with aldehydes other than formaldehyde. Formaldehyde itself does form ene adducts, even with mono- and 1,2-disubstituted alkenes, in good yields. When only one equivalent of the catalyst was used, chloro-alcohols were formed, whereas with 1.5 to 2 equivalents, ene products predominated.

In contrast, ethylaluminium dichloride is a stronger Lewis acid with a less nucleophilic alkyl group. Therefore the problem of alkyl addition to the enophile is reduced. This catalyst gives good yields of ene adducts even with the less reactive 1,2-disubstituted alkenes and formaldehyde with no formation of chlorinated side products or alkyl additions.<sup>40</sup> The presence of functional groups (*eg.* acetate) does not restrict the synthesis, but a second equivalent of catalyst must be used to allow for complexation to the basic substituent.

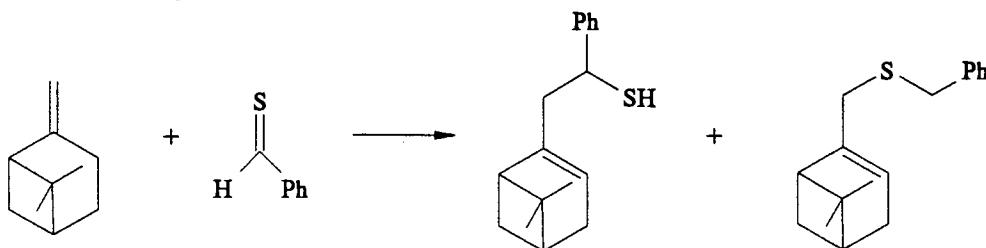
Product distributions (and mechanisms<sup>38</sup>) may vary between thermal and catalysed reaction.<sup>41</sup> For example, in the addition of diethyl oxomalonate to 6-methylhepta-1,5-diene (Scheme 12), the dominant product is reversed between the two reaction modes.



**Scheme 12**

### 1.3.4 Sulfur containing enophiles

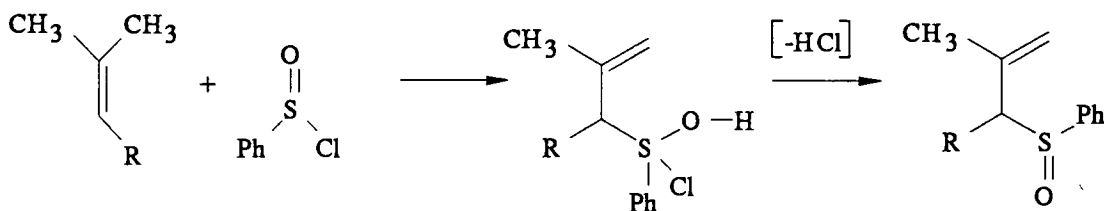
With thioaldehydes the formation of both C-C and C-S bonds has been demonstrated.<sup>42,43</sup> Eg. with  $\beta$ -pinene and thiobenzaldehyde Baldwin and Lopez reported a 2:1 mixture of regioisomers (Scheme 13). However, with the less reactive alkene, cyclododecene, the ene reaction failed and starting material was recovered.



Scheme 13

Thioketones and the thione group of the dithio ester, methyl cyanodithioformate ( $\text{NCCS}_2\text{Me}$ ), have also been reported<sup>44</sup> to react.

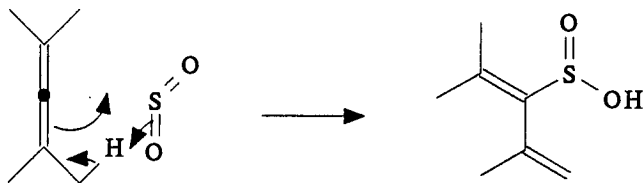
Benzenesulfinyl chloride adds to alkenes to form allylic sulfoxides,<sup>45</sup> presumably after elimination of HCl (Scheme 14).



Scheme 14

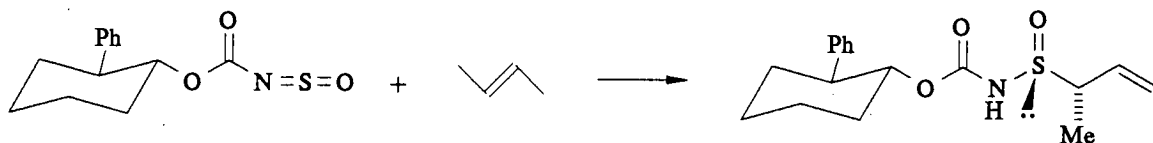
Meth-Cohn and Vuuren have described the synthesis<sup>46</sup> and ene additions<sup>47</sup> of electron poor thionitroso compounds ( $\text{R-N=S}$ , where  $\text{R} = \text{CO}_2\text{Et}$ ,  $\text{CO}_2\text{Ph}$ ,  $\text{ArSO}_2$ ). The generation of these thionitroso systems involves cycloaddition of the relevant tetrachlorothiophene-S,N-ylide to anthracene, releasing the enophile which is then free to undergo ene additions to form acylthiohydroxyamines.

The cumulene systems,  $\text{N}=\text{S}=\text{O}$ ,  $\text{N}=\text{S}=\text{N}$ ,  $\text{C}=\text{C}=\text{S}$ <sup>48</sup> and  $\text{O}=\text{S}=\text{O}$  have been studied. Sulfur dioxide functions as an enophile, for example forming a sulfinic acid on addition to tetramethylallene at room temperature<sup>49</sup> (Scheme 15).



Scheme 15

*N*-Sulfinylarenesulfonamides,  $\text{ArSO}_2\text{N}=\text{S}=\text{O}$ , have been described by Kresze *et al* as superenophiles.<sup>50</sup> The perfluorobutane analogue ( $\text{C}_4\text{F}_9\text{SO}_2\text{N}=\text{S}=\text{O}$ ) is more reactive still<sup>51</sup> ( $\times 10^3$ - $10^4$ ) and even reacts with electron deficient enes, such as 1-chloro-2-methyl-1-propene. The *N*-sulfinylcarbamate in Scheme 16 adds to *trans*-2-butene with  $\text{SnCl}_4$  catalysis<sup>52</sup> to give an optically active product, at both carbon (S) and sulfur (R).

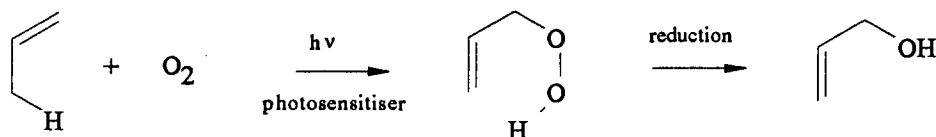


Scheme 16

Symmetrical and non-symmetrical diimides such as *N,N'*-ditosylsulfurdiimide ( $\text{Tos-N}=\text{S}=\text{N-Tos}$ )<sup>53,54</sup> and *N*-aryl-*N'*-tosylsulfurdiimide ( $\text{Ar-N}=\text{S}=\text{N-Tos}$ )<sup>54</sup> undergo additions to their  $\text{N}=\text{S}$  bonds; in the latter case (where aryl =  $\text{C}_6\text{F}_5$ ), the addition takes place selectively at the  $\text{ArN}=\text{S}$  bond. This was rationalised with the aid of an X-ray structure determination which showed that the  $\text{ArN}=\text{S}$  bond is *Z*-configured (and therefore better orientated to take part in the ene reaction) whereas the  $\text{TosN}=\text{S}$  possesses the *E* configuration.

### 1.3.5 Singlet oxygen

Oxygen, in its first excited state ( $^1\text{O}_2$ ), is a powerful enophile which adds to unsaturated compounds to form allyl hydroperoxides. These peroxides are unstable but can be readily reduced to the corresponding allyl alcohols by sodium borohydride, lithium aluminium hydride, triphenylphosphine or organic phosphites (Scheme 17).



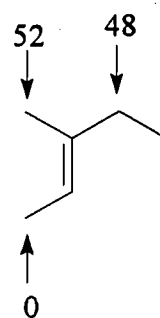
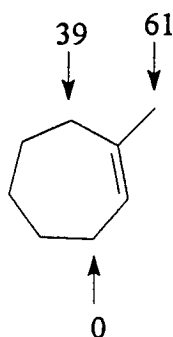
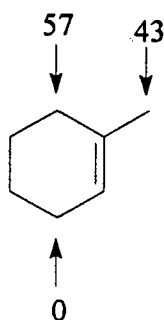
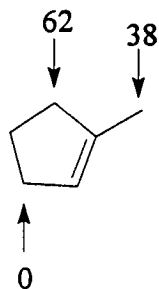
Scheme 17

Similarities between the ene mechanisms for singlet oxygen and PTAD have been highlighted in the literature.<sup>10,14,20</sup> Both reactions are thought to proceed through similar intermediates: perepoxides and aziridinium imides, respectively. Product selectivities, however, can be markedly different; *eg.* with tri-substituted alkenes, PTAD selectively abstracts allylic hydrogens from the more substituted end of the double bond, whereas singlet oxygen shows more preference for abstraction from the more substituted *side* rather than the more substituted *end*. Scheme 18 compares the proportions (%) of hydrogen abstraction sites from a series of alkenes for PTAD *versus* singlet oxygen.

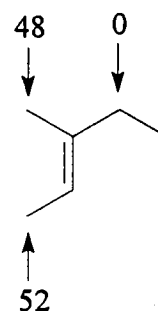
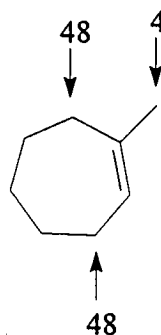
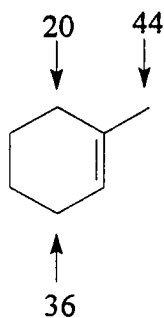
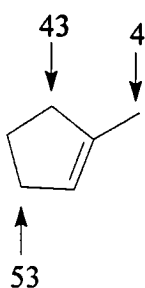


## Hydrogen Abstraction Sites /%

With PTAD:



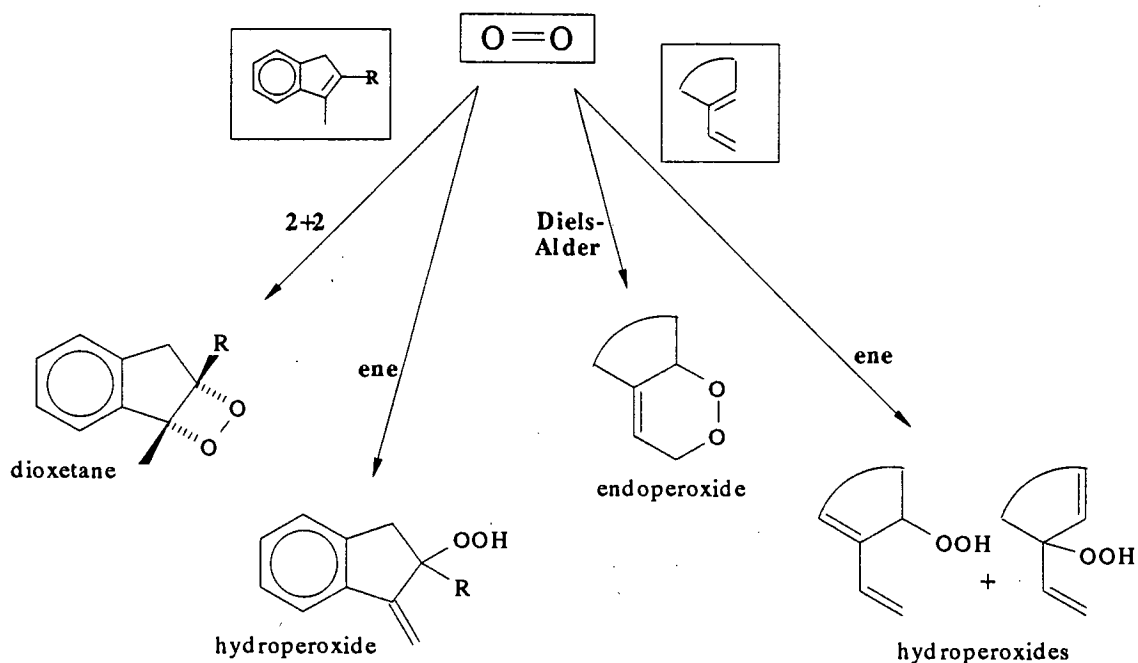
With Singlet Oxygen:



Scheme 18

Several theoretical studies have been made on the ene addition of  $^1\text{O}_2$ , but these calculations are often inconsistent and their predictions are conflicting; Houk<sup>55</sup> concluded that a concerted process was preferred while Dewar and Thiel<sup>56</sup> calculated that perepoxide formation was energetically favoured. Yet another group (Harding and Goddard<sup>57</sup>) favoured the diradical intermediate mechanism.

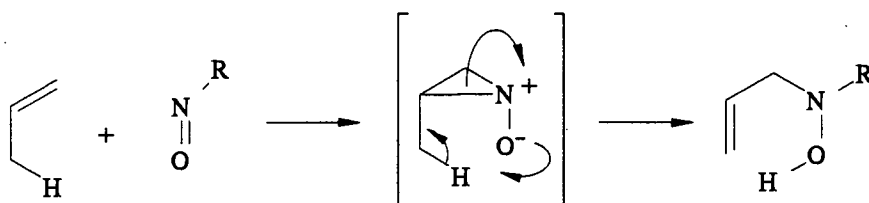
[2+2] Cycloaddition of singlet oxygen, to form dioxetanes, can compete with the ene reaction, as can the Diels-Alder cycloaddition if the substrate is a 1,3-diene (to form endoperoxides). These competing reactions are illustrated in Scheme 19. The photooxidation of indenenes<sup>58</sup> affords dioxetanes as the major products, while 1-vinylcycloalkenes react with singlet oxygen<sup>59</sup> to form endoperoxides by Diels-Alder cycloaddition as well as two types of hydroperoxides *via* the ene reaction.



Scheme 19

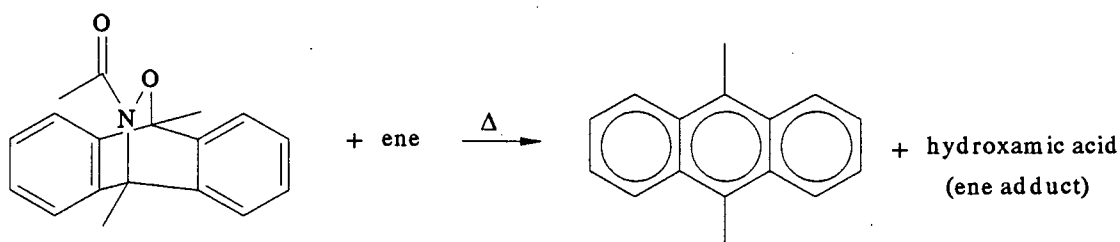
### 1.3.6 Other Enophiles

Various other heteroenophiles have been investigated.<sup>60-64</sup> For example, nitroso compounds react with simple olefins *via* formation of an aziridine *N*-oxide (or a similar species with the same structural characteristics)<sup>60</sup> to form hydroxylamines (Scheme 20).



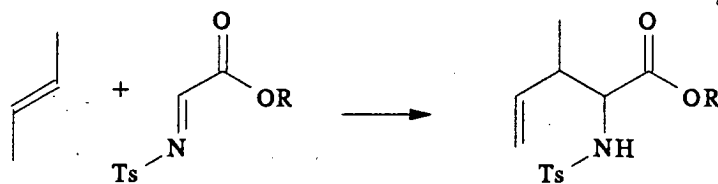
Scheme 20

Acylnitroso compounds have been generated by thermal liberation from their Diels-Alder adducts (with 9,10-dimethylantracene) in the presence of the ene component (Scheme 21) and their use as enophiles has been reviewed by Keck *et al.*<sup>61</sup>



Scheme 21

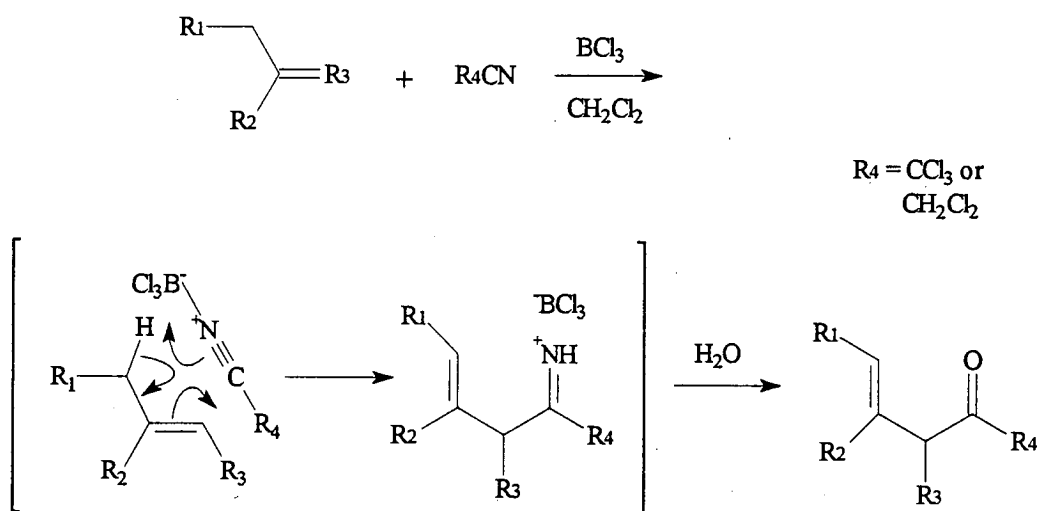
Activated imines, such as *N*-sulfonylimines (Tos-N=CH-CO<sub>2</sub>R; R = Bu, Et) undergo highly selective ene additions to cyclohexane and *trans*-2-butene<sup>62</sup> (Scheme 22). The products from an endo transition state are dominant in both cases. Braxmeier and Kresze<sup>63</sup> have also used substituted sulphonylimines as enophiles.



**Scheme 22**

A phosphalkyne ( $\text{P}\equiv\text{C}^t\text{Bu}$ ) has been shown to undergo ene addition under pressure to a sterically crowded pentadiene (pentamethylcyclopentadiene).<sup>64</sup>

Nitriles are a further example of triply bonded enophiles. The reaction of trisubstituted alkenes with trichloroacetonitrile or dichloroacetonitrile in the presence of  $\text{BCl}_3$  has been reported.<sup>65</sup> The products were  $\beta,\gamma$ -unsaturated ketones in high yields (*ca.* 70 %, Scheme 23).

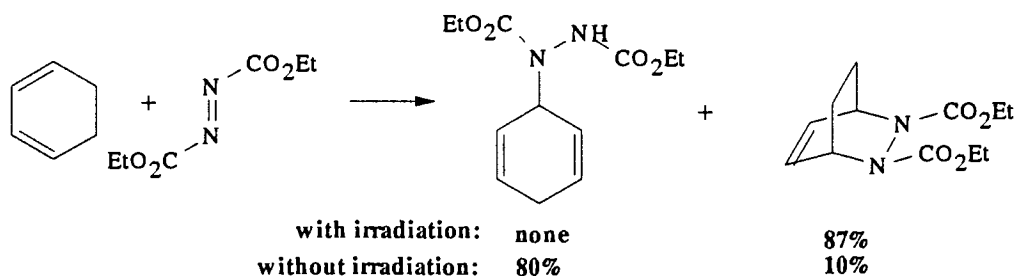


**Scheme 23**

## 1.4 The Ene Component

Enes are  $\pi$ -bonded molecules that contain an allylic hydrogen which is available for abstraction in the reaction. As has been seen in the previous section, simple alkenes have been extensively used; including terminal, cyclic, exo-cyclic, *cis* and *trans* mid-chain and branched examples. Although the exact order depends on the reaction conditions and enophile, the typical relative reactivity for alkenes has been found to be 1,1-di > tri > tetra >> mono > 1,2-disubstituted.<sup>66</sup>

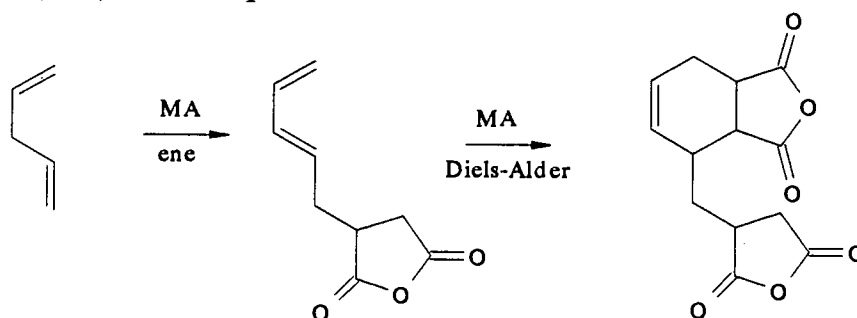
1,3-Dienes can undergo both ene and Diels-Alder additions. The balance between the two pathways is dependant on several factors, including the configuration of the enophile. The reaction of cyclohexadiene with DEAD gives the ene adduct as the major product<sup>67</sup> whereas, on irradiation, the DEAD forms its Diels-Alder cycloadduct exclusively<sup>68</sup> *via* generation of its *cis* isomer (Scheme 24). The *trans* geometry of DEAD, before irradiation, is an unfavourable arrangement for the Diels-Alder cycloaddition and so the ene reaction is able to compete, whereas, after irradiation, the lower energy requirements of the Diels-Alder reaction dominate the competition.



Scheme 24

Steric factors are also important in determining the balance between ene and Diels Alder adducts. Alkenes such as 2,5-dimethyl-2,4-hexadiene and 2,4-dimethyl-2,4-pentadiene react to give only ene adducts with benzyne and DEAD respectively.<sup>7</sup> Transoid 1,3-dienes cannot form Diels-Alder adducts and only undergo ene reactions.

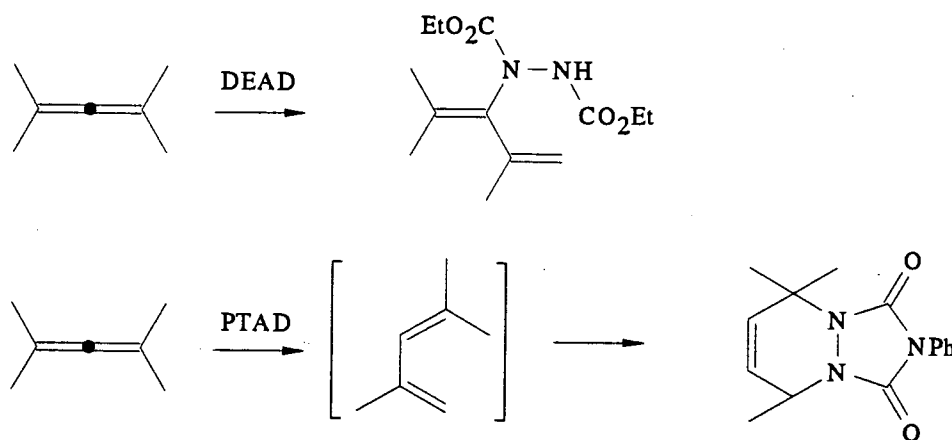
One of the products from ene addition to 1,4-dienes is a conjugated 1,3-diene resulting from the allylic bond shift. This can then react further by a second ene addition, or a [4+2] cycloaddition if the enophile is also a good dienophile. Scheme 25 shows such a tandem ene/Diels-Alder sequence for maleic anhydride (MA) with 1,4-pentadiene.<sup>69</sup>



Scheme 25

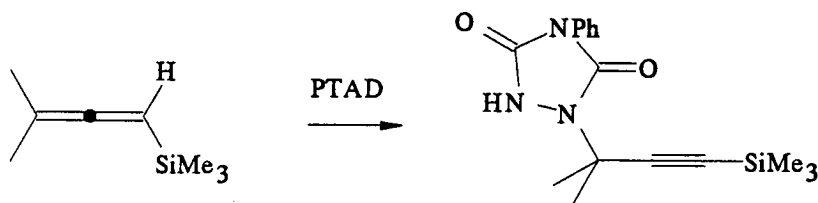
Conjugated trienes can also take part in the reaction. Alkynes, on the other hand, are poor ene components; benzyne reacts with 1-hexyne to give only 4% of the allene ene product.<sup>7</sup>

Alkyl allenes are attacked at the central carbon atom to form 1,3-dienes.<sup>70</sup> For example, tetramethylallene reacts with DEAD to form the ene adduct in 94% yield. In contrast, with PTAD, a Diels-Alder adduct was formed in 89% yield. The authors proposed a rearrangement of the allene to the isomeric conjugated diene to allow the cycloaddition (Scheme 26).



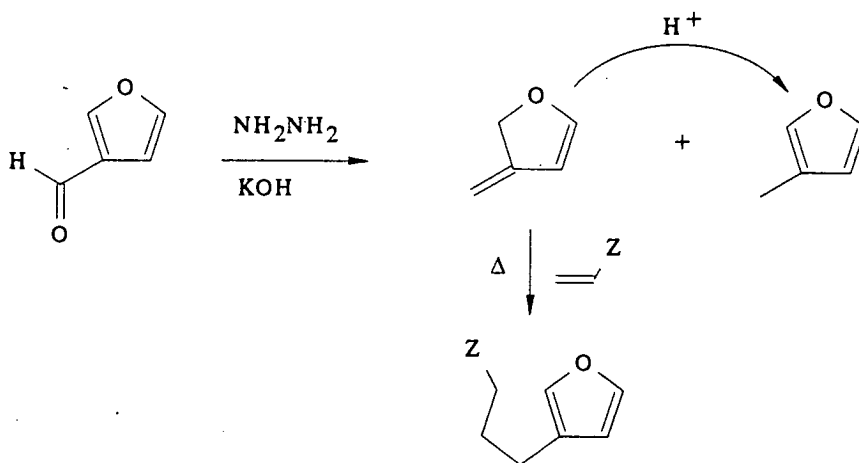
Scheme 26

Allenyl silanes react differently from above;<sup>71</sup> the hydrogen  $\alpha$  to the silicon is abstracted with both PTAD and  $\text{PhSO}_2\text{NSO}$  to form acetylenes rather than 1,3-dienes (Scheme 27).



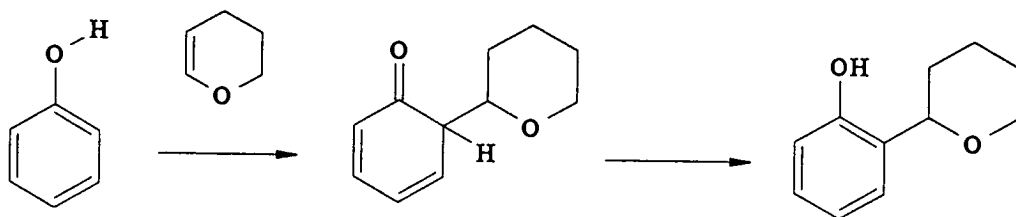
Scheme 27

The ene reaction has been employed both in creating aromatic rings and in utilising them as ene components. For example the reaction of 3-methylene-2,3-dihydrofuran (generated from 3-furaldehyde by the Wolff-Kishner reduction) with mono-substituted enophiles gives 3-substituted furans<sup>72</sup> (Scheme 28).



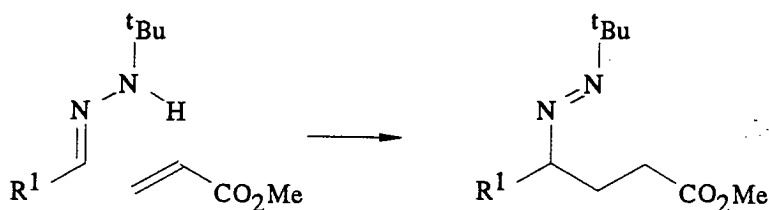
Scheme 28

An example of an aromatic system being used as the ene unit is the reaction of phenol with dihydropyran<sup>73</sup> (Scheme 29).



Scheme 29

There was no competing *para* substitution as the ene reaction was controlling the addition. This is also an example of a carbon-hetero atom ene component, a further case being the use of *t*-butyl- and phenyl-hydrazones of aliphatic aldehydes.<sup>74</sup> Scheme 30 shows the formation of a  $\gamma$ -azoester on reaction with methyl acrylate. Addition of acrylonitrile furnished the corresponding nitrile.



Scheme 30



## 1.5 Intramolecular Ene Reactions

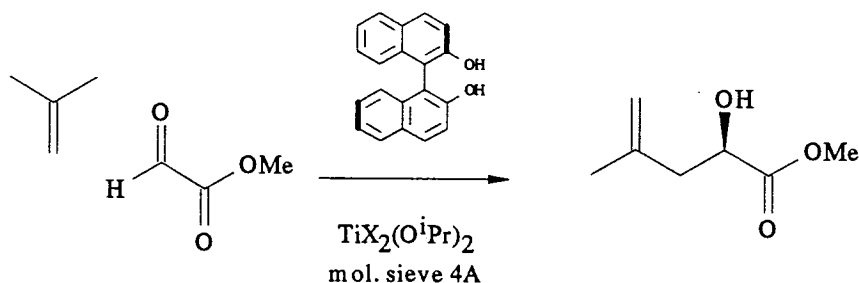
Intramolecular ene reactions have often been utilised in natural product syntheses and can be considered as three variants depending on whether the enophile is linked to the olefinic terminal, the central atom, or the allylic terminal of the ene component. Oppolzer and Snieckus<sup>75</sup> have systematically reviewed the three types, the first being by far the most common. These reactions can exhibit useful regio- and stereochemistry as well as being favoured in terms of entropy.

## 1.6 Organometallic Ene Reactions

Organometallic compounds have previously been mentioned in their capacity as ene components<sup>71</sup> and as enophiles ( $C\equiv P^{64}$ ). Furthermore, the vinyl derivatives  $C=CMX_3$  (where  $M = Si$  or  $Ge$ ) as well as silenes and germenenes ( $M=C$ ) are all reactive. Ene and retro-ene reactions involving Group 14 organometallic compounds have been the subject of a comprehensive review.<sup>76</sup>

## 1.7 Asymmetric Ene Reactions

Chiral Lewis acids, usually generated *in situ* from a Lewis acid and a chiral auxiliary, have been effectively applied to perform asymmetric ene reactions, both inter- and intra-molecularly. For example, the addition of methyl glyoxylate to terminal alkenes proceeds enantioselectively (with 83-95% ee)<sup>77</sup> to provide  $\alpha$ -hydroxy esters when titanium dihalides containing a chiral binaphthol group and molecular sieve are present (Scheme 31).

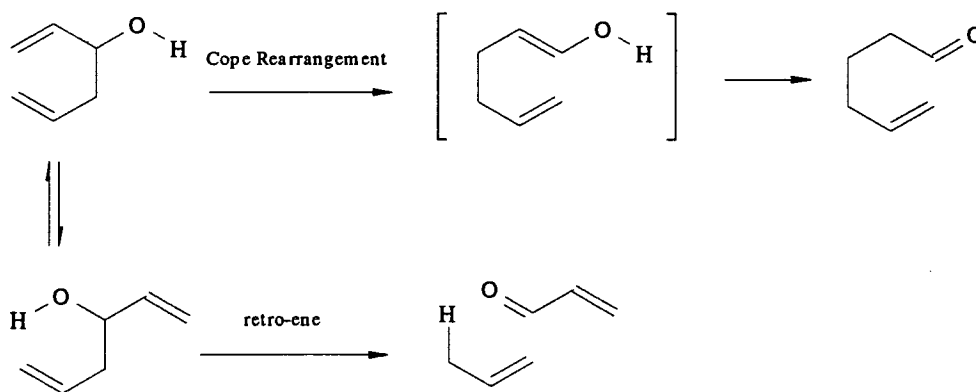


Scheme 31

The use of chiral Lewis acids to promote asymmetric intramolecular reactions is discussed in a review by Narasaka.<sup>78</sup>

## 1.8 Retro-Ene Reactions

The thermal reversion of the ene reaction can be utilised as a method for accessing unsaturated, reactive molecules. Flash vacuum thermolysis techniques are often employed, but the reversion can also be accomplished by refluxing in an inert solvent. The synthetic applications of the retro-ene reaction were recently reviewed by Ripoll and Vallee,<sup>79</sup> and the topic has been covered in several of the other reviews previously mentioned.<sup>2,6,7,9</sup> As with the forward reaction, no common mechanism governs all the retro-ene reactions and the pathways have been described as both concerted and radical. Heteroatoms, such as oxygen, nitrogen, sulphur and silicon are often present among the six centres involved in the reaction. In the case of 3-hydroxyhexa-1,5-diene, it has been reported that the Cope rearrangement (a 3,3-sigmatropic shift) competes with the retro-ene fragmentation (Scheme 32).



Scheme 32

## 1.9 Objectives of Research

The aims of this work were to modify vegetable oils by the addition of a variety of enophiles, thus introducing functionality into lipophilic molecules. Such compounds show potential in lubrication; particularly as boundary friction reduction and extreme pressure additives.

Before attempting modification of the oils themselves, preliminary studies were carried out on simple alkenes and unsaturated esters, both to establish the reaction conditions and to provide well defined model systems for comparison purposes. The model adducts were designed to aid the characterisation of the modified oils as, by their nature, the oils are composed of a mixture of components and consequently give rise to complex products.

The range of enophiles which were employed in this research includes three azo compounds (the triazolinediones, PTAD and MTAD, and diethyl azodicarboxylate, DEAD); a simple aldehyde which was activated by Lewis acid catalysis (formaldehyde), and a sulfinyl sulfonamide (*p*-toluenesulfinyl sulfonamide).

Subsequent chapters of this thesis will describe the reactions carried out on jojoba oil, on other vegetable oils and on synthetic fluids. Each of these three chapters will contain an introductory section (describing the structure, uses and chemistry of the ene component) followed by discussion of the work carried out. The latter sections fall naturally into subdivisions according to the enophile *ie.* azo compound, formaldehyde or sulfinyl compound.

## 2. JOJOBA OIL

### 2.1 Introduction to Jojoba Oil

Jojoba (botanical name *Simmondsia chinensis*) is a desert shrub native to southern Arizona and northwest Mexico. It has waxy leaves and a long tap root and so is well-adapted to the harsh conditions of extreme temperature fluctuations, poor soil quality and limited moisture, which make these areas generally unsuitable for agricultural crops. Italy, Spain, Australia and many South American and African countries have invested in commercial plantations<sup>80a</sup> and jojoba has successfully been introduced to the Negev desert by researchers at the Ben-Gurion University in Israel who have been actively studying its uses and modifications over the last 20 years. Much of this research has been described Wisniak in his book 'The Chemistry and Technology of Jojoba Oil'.<sup>81</sup> There have also been seven 'International Conferences on Jojoba and its Uses', the first in 1972, in each of which the plant physiology, agronomy, processing, economics, marketing, chemistry, and uses have been discussed.<sup>82</sup> There follows a brief overview of the structure, uses (with emphasis on lubricant applications), and basic chemistry which has been carried out on jojoba oil.

#### 2.1.1 Structure of Jojoba Oil

Jojoba is unique in that the seeds of the plant contain nearly 50% by weight of an oil whose structure is not that of a triglyceride (or fat), instead it is a wax ester composed mainly of the straight chain esters of  $C_{20}$  and  $C_{22}$  monounsaturated acids and alcohols. As can be seen from Figure 1, jojoba oil is composed of a mixture of chain lengths but the major constituents are docosenyl and eicosenyl eicosenoates ( $n = 12, 10$  and  $m = 9$ ). Miwa and Spencer found,<sup>83</sup> using GLC, HPLC, mass spectroscopy and ozonolysis, that batches of oil from the Sonora desert and coastal California tended to have slightly higher molecular weights than those from Arizona and Israel.

However, within any region, the composition is remarkably constant. For the purposes of this thesis the structure will be represented by the component where  $m = 9$  and  $n = 12$ . This is the major component, typically comprising *ca.* 40% of the total,<sup>81</sup> and has a formula weight of 616.

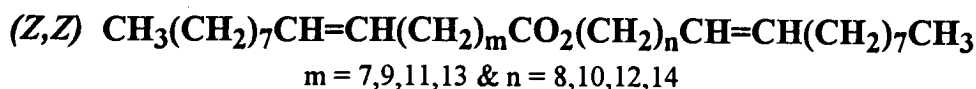


Figure 1

The banning of sperm whale oil products in the late seventies led to a hunt for a replacement. The structures of typical components of jojoba and sperm whale oil are similar (Figure 2) and contrast with those of a typical vegetable oil. There are, however, differences in composition between them. Sperm whale oil contains 82-85% by weight of wax esters plus 12-15% of glyceride esters. In jojoba these triglycerides are present in less than 1%. Jojoba was found to be an excellent substitute in lubricant applications for several reasons:<sup>84</sup> it does not darken and remains liquid, even when highly sulfurised (while the whale oil required the addition of mineral oil); it has no fishy odour and - as the crude oil contains >97% of linear wax esters - needs little purification for most industrial purposes.

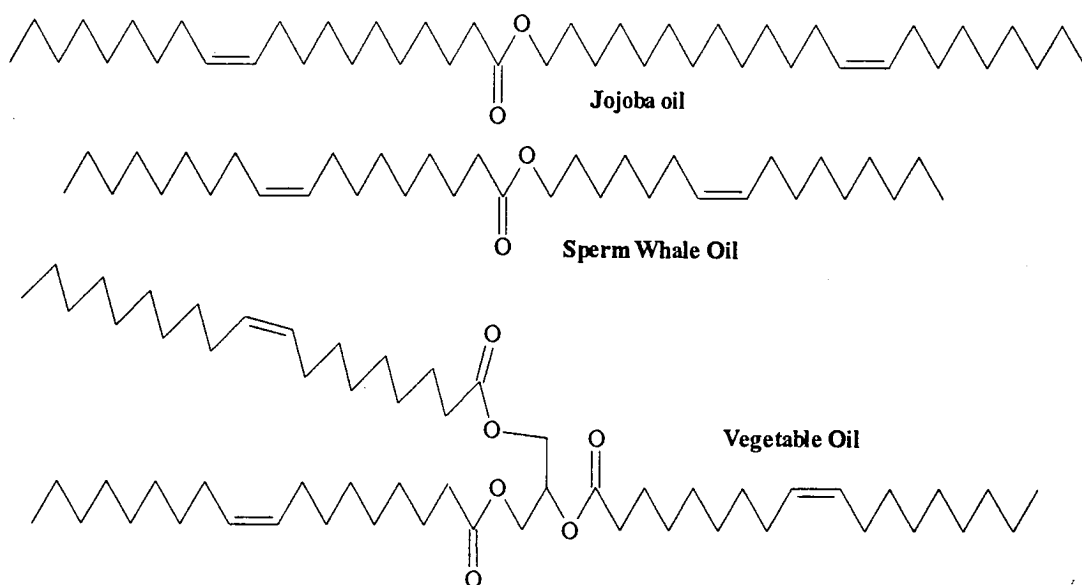
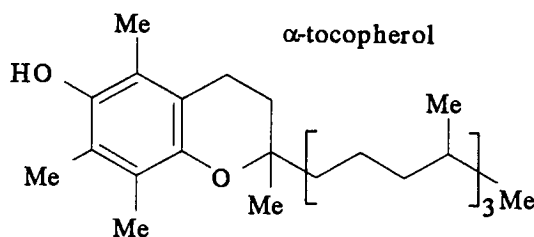


Figure 2

Jobaba oil is unusually stable towards oxidation. This has been attributed<sup>85</sup> to the presence of small quantities (<60 ppm) of tocopherols which act as natural antioxidants.



**Figure 3**

### 2.1.2 Uses of Jojoba Oil

In the past, American Indians ground up jojoba nuts to form a paste which they used as a hair oil. They also used it for cooking and as an ointment. The cosmetic industry today is a major user of jojoba oil; it appears in a wide range of products and especially in hair care applications. In 1989 the Food and Drug Administration (FDA) records showed that jojoba oil was registered as a component in 188 cosmetic products with concentrations ranging from 0.1 to 25%. The Journal of the American College of Toxicology recently published their final toxicity assessment on jojoba<sup>86</sup> which confirmed that the oil is a safe cosmetic ingredient in the present levels of use and concentration. Patents have been taken out to cover a variety of uses, including: hypocalorific foods,<sup>87</sup> as the oil cannot be totally digested (a drawback to this is the presence of  $C_{20}$  and  $C_{22}$  monoene components which are known to be an undesirable component in the diet),<sup>79</sup> an additive to reduce foaming during antibiotic production,<sup>88</sup> and a drug coating to allow passage of drugs through the stomach and into the small intestine before release.<sup>89</sup> Jojoba oil is also a good source for the unusual, long-chain,  $C_{20}$  and  $C_{22}$  monounsaturated alcohols and acids which can be used in the manufacture of wetting agents, detergents and sulfated products.

The search for a sperm whale oil replacement for lubricant applications, coupled with both the desire to develop products which do not depend on crude oil, and environmental pressure to find biodegradable alternatives<sup>90,91</sup> has led to an upsurge of interest in jojoba. Tests have been carried out<sup>92,93</sup> to assess jojoba (and sulfurised jojoba) for oxidative stability, viscosity index, rust protection, friction modification and foaming and wear characteristics. The materials have been tested as solutions in mineral oil base fluids as well as in their pure states. Bhatia *et al*<sup>94</sup> have formulated gear oils and extreme pressure additives from sulfurised jojoba which surpass industry standard specifications, while the Dow Chemical Company has also found sulfurised jojoba to be an excellent extreme pressure additive.<sup>95</sup> Jojoba has a higher viscosity index than most mineral oils. This is a measurement of the change in viscosity with temperature. Jojoba's high index is beneficial in lubrication because it results in less viscous drag when the oil is cool during equipment start-up, yet still provides thick films when the oil is warm. A problem with jojoba is its high pour-point (12-17°C), that is the temperature at which the oil starts to solidify. This means that its uses are confined to high temperature applications, unless it is used in conjunction with a pour-point depressant.<sup>96</sup>

The major drawback to the use of jojoba in place of sperm whale oil is its higher cost in comparison to substitutes derived from other sources.<sup>97</sup> Workers in Spain have recently optimised the synthesis of oleyl oleate (from oleic acid and oleic alcohol) as a jojoba oil substitute, using cobalt chloride as catalyst.<sup>98-100</sup> This synthesis is attractive because of the low cost and good availability, in Spain, of the starting lipids, as they are readily accessible from olive oil. The same workers also describe this esterification using zeolites as catalysts.<sup>101</sup> The authors claim that this method reduces the possibility of metal contamination from the catalyst. The zeolites show a shape selective effect as they do not catalyse the reaction to form esters containing 38 or more

carbon atoms. An enzymatic synthesis of a jojoba analogue has also been described<sup>102</sup> using *Mucor meihei* lipase immobilised on a macroporous exchange resin (Lipozyme).

Another alternative to jojoba oil is Orange Roughy oil which is extracted from a fish found in New Zealand waters. This oil is also a wax ester, mainly composed of C<sub>16</sub>-C<sub>22</sub> acids and alcohols and containing about 5% of triglycerides. The main fatty acid components of the swim bladder (which contains over 60% lipid) are<sup>103</sup> 18:1 (54%), 20:1 (17%), 16:1 (13%), and 22:1 (8%) while the fatty alcohols are also predominantly mono-unsaturated but contain a significant amount (33%) of saturates. Although the liver and the roe of the fish contain up to 26% of polyunsaturates (22:6), these comprise a small fraction<sup>104</sup> (<3%) of the lipid total. The extraction of the fish oils has been commercialised in New Zealand; in 1985 there were five orange roughy plants, which mostly export to Japan, Europe and Australia.<sup>105</sup>

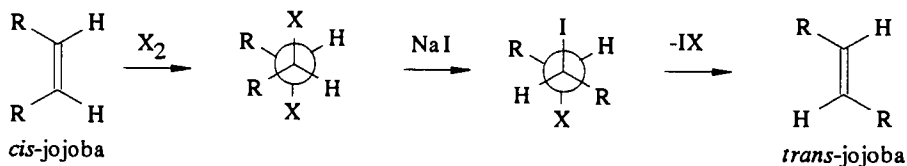
### 2.1.3 Chemical Modifications of Jojoba Oil

Wisniak's book,<sup>81</sup> which was published in 1987, describes the chemistry which had been carried out on jojoba up until that date and in earlier work within our Edinburgh research group (on 1,3-dipolar cycloadditions<sup>106</sup>) the reactions on jojoba up to 1990 were reviewed.<sup>107</sup> These modifications will be summarised here and the more recent developments will be described.

The majority of chemical reactions on jojoba have been carried out on the unsaturated portion of the molecule *via* electrophilic addition to the alkene unit. The associated allylic positions have also been modified, while typical reactions occur at the ester function including hydrolysis, aminolysis and transesterification.

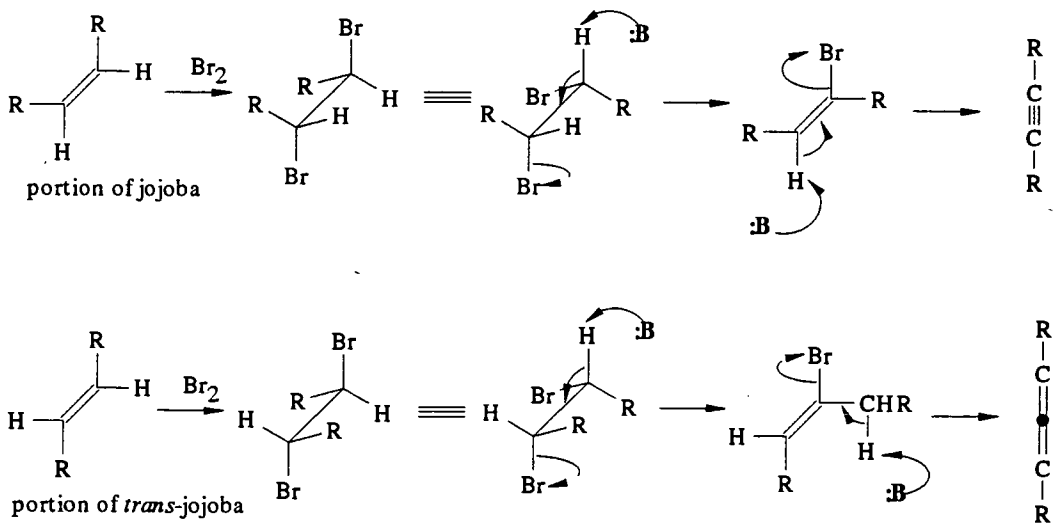


Isomerisation from *cis* to *trans* geometry, which raises the melting point, can be carried out by a number of routes: thermal<sup>108</sup> (initiated by bentonite clays), photochemical<sup>109</sup> or using a catalyst,<sup>110</sup> such as selenium and the oxides of nitrogen. By these methods the reaction reaches an equilibrium concentration of about 60-75% *trans*. A different approach was taken by Shani<sup>111</sup> in his preparation of all *trans*-jojoba by the anti addition of bromine or chlorine to the double bonds, followed by an S<sub>N</sub>2 displacement with sodium iodide and anti-elimination (Scheme 33). The melting point of this compound was 50-52°C. Catalytic hydrogenation<sup>112</sup> of the alkene units also raises the melting point and improves the oxidative stability of the oil.



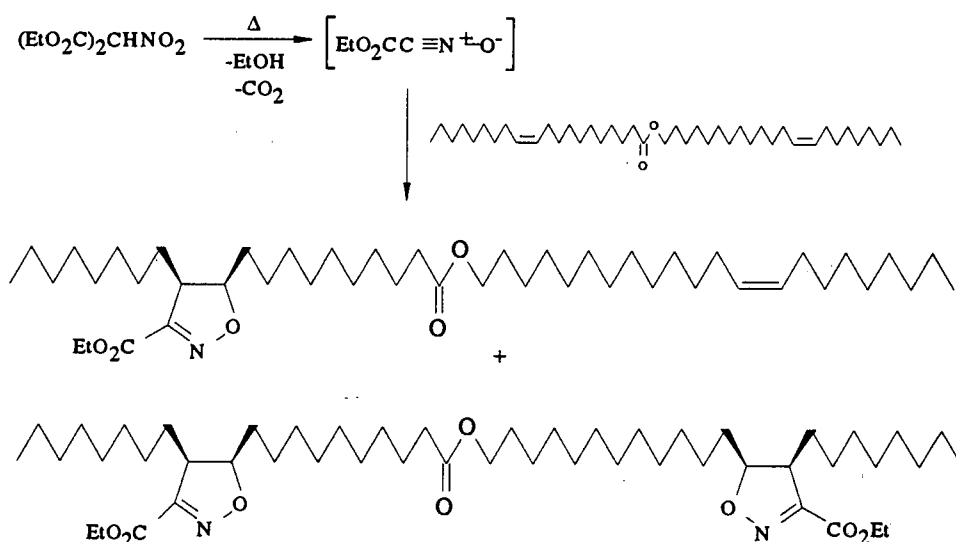
### Scheme 33

Addition of bromine to jojoba oil and its *trans* isomer yielded tetrabromojobaba<sup>113</sup> which afforded acetylenic and allenic components, respectively, on treatment with base (Scheme 34). Under these conditions some hydrolysis of the ester was also observed.



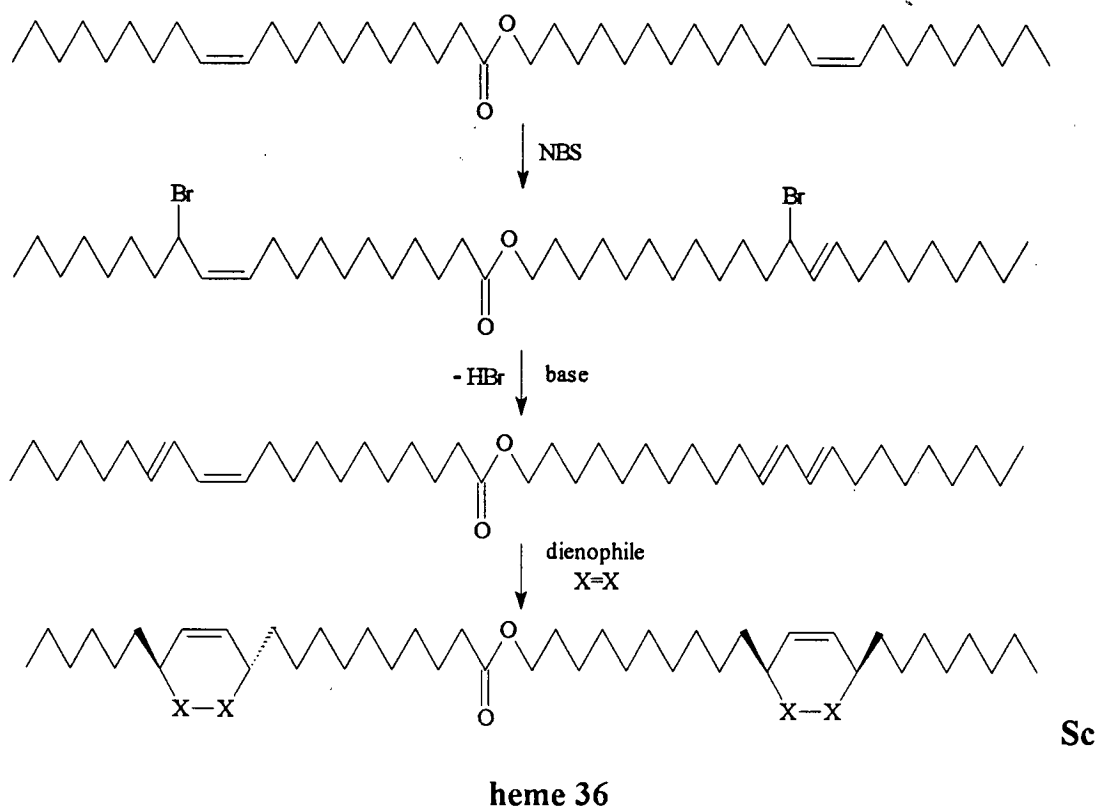
### Scheme 34

Jojoba has also been used as a dipolarophile component in 1,3-dipolar cycloaddition reactions.<sup>106</sup> Ethoxycarbonylformonitrile oxide was selected as the dipole as it is activated by electron withdrawing groups towards cycloaddition with the electron rich alkenes and it can be conveniently generated from diethyl nitromalonate. Cycloaddition afforded a mixture of mono- and di-isoxazoline adducts with *cis*-4,5-disubstituted geometry. This is illustrated in Scheme 35. For reasons of clarity and brevity, only one regioisomer is shown here and in subsequent schemes.



Scheme 35

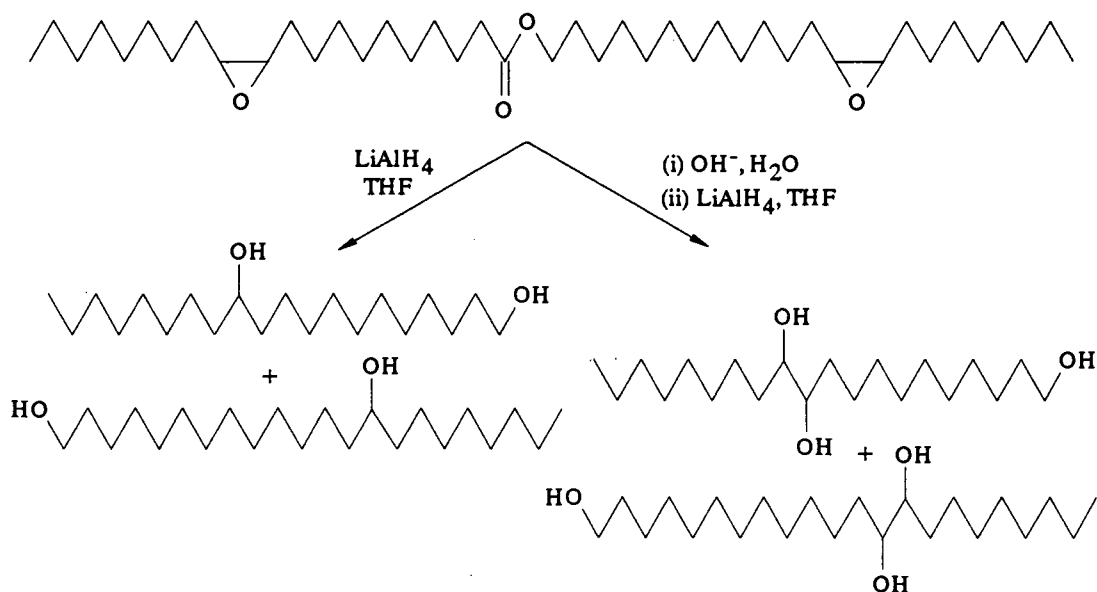
Conjugated dienes have been prepared<sup>114</sup> *via* allylic bromination of jojoba using NBS followed by base induced elimination of hydrogen bromide. Isomerisation to *ca.* 65% *trans* took place during the bromination step and so, on treatment with lithium carbonate and lithium chloride in an aprotic solvent, a mixture of *E,E* and *E,Z* conjugated dienes was produced. These features are illustrated in Scheme 36. Diels-Alder products derived from the jojobatetraenes with several dienophiles (maleic anhydride, *N*-methylmaleimide, acrylonitrile and singlet oxygen) introduced more functionality into the oil, allowing further derivitisation of jojoba.



Allylic bromination, using four equivalents of NBS, followed by hydrogen bromide elimination afforded jojobahexaene.<sup>115</sup> The highly brominated dodecabromojjoba and octabromojjoba, which have potential as fire-retardant additives because of their high densities, were also synthesised<sup>115</sup> by the addition of bromine to jojobahexaene and jojobatetraene.

In the search for plasticisers, jojoba has been "maleinised".<sup>116</sup> The addition of maleic anhydride can take place by an ene reaction or, as the reaction temperatures are high, by a free radical mechanism. Epoxidised jojoba (synthesised by the action of peroxyacetic acid solution in acetic acid) has been tested as a thermal and ultraviolet light stabiliser, but was found to be unsuitable as a primary plasticiser as it was incompatible with the vinyl copolymers studied.<sup>117</sup> Similar conclusions were reached in another study<sup>118</sup> in which *m*-chloroperoxybenzoic acid had been used to epoxidise the oil. Landis *et al*<sup>119</sup> also used the epoxidised oil to produce monohydroxyjojoba alcohols

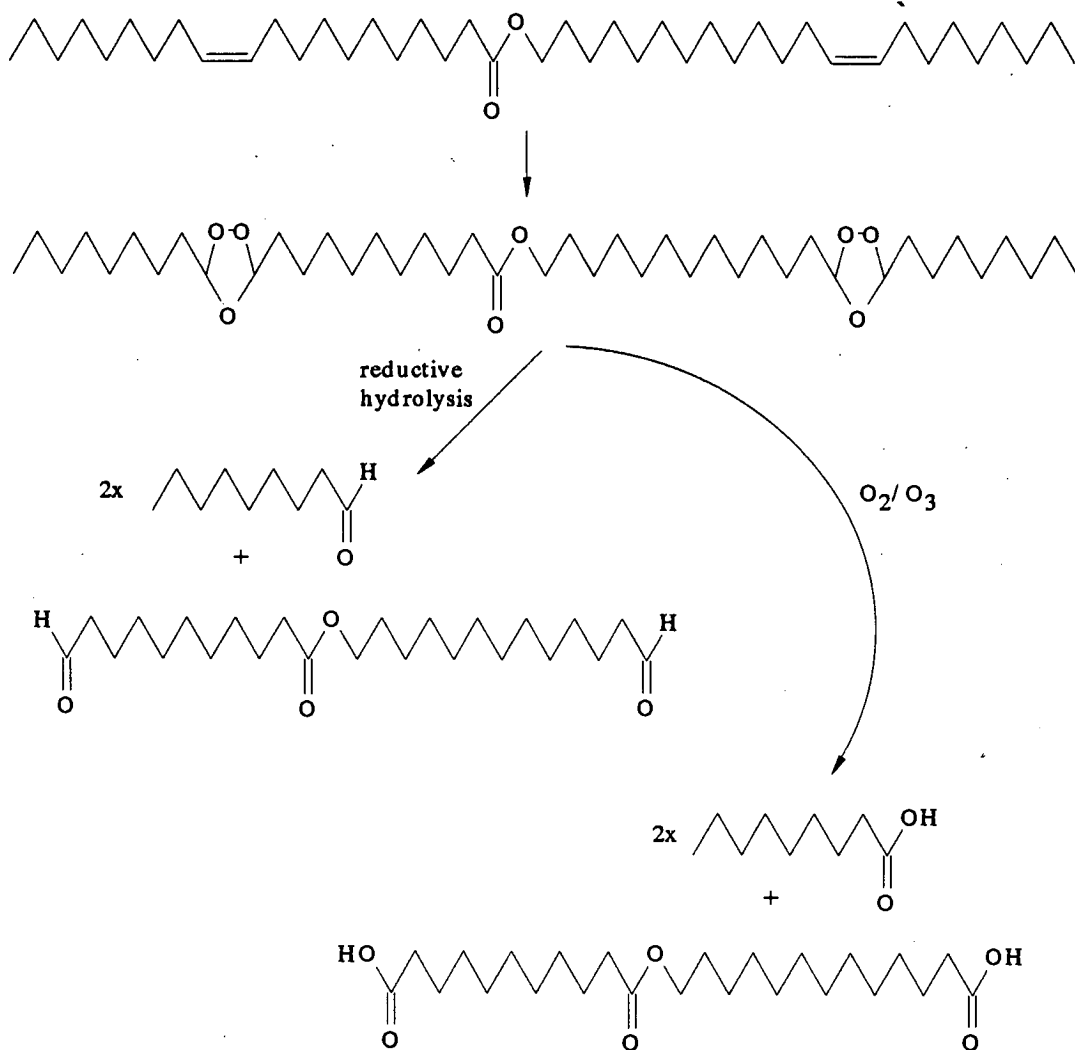
(after reduction with lithium aluminium hydride). Alternatively, hydrolysing the diepoxide with dilute base before reduction gave a route to the dihydroxyjojoba alcohols (Scheme 37).



Scheme 37

Other reactions on the double bonds include: sulfurisation,<sup>84,120</sup> sulfur chlorination<sup>121</sup> and sulfur bromination<sup>122</sup> to produce materials which are claimed to have superior properties as lubricant additives, especially in extreme-pressure load carrying applications. Using *tert*-butyl perbenzoate as a radical generator, Wisniak has phosphonated jojoba oil<sup>123</sup> and has also carried out sulfur phosphorilation using diphosphorous pentasulfide.<sup>124</sup>

Ozonolysis is a common technique employed in the analysis of unsaturated compounds. Ozonides are also valuable intermediates for many synthetic paths, yielding for example dialdehydes and diacids on reductive hydrolysis or further oxidation respectively<sup>125</sup> (Scheme 38). Another route to the diacid is the direct oxidation of jojoba using potassium permanganate<sup>126</sup> which is carried out under phase transfer conditions.

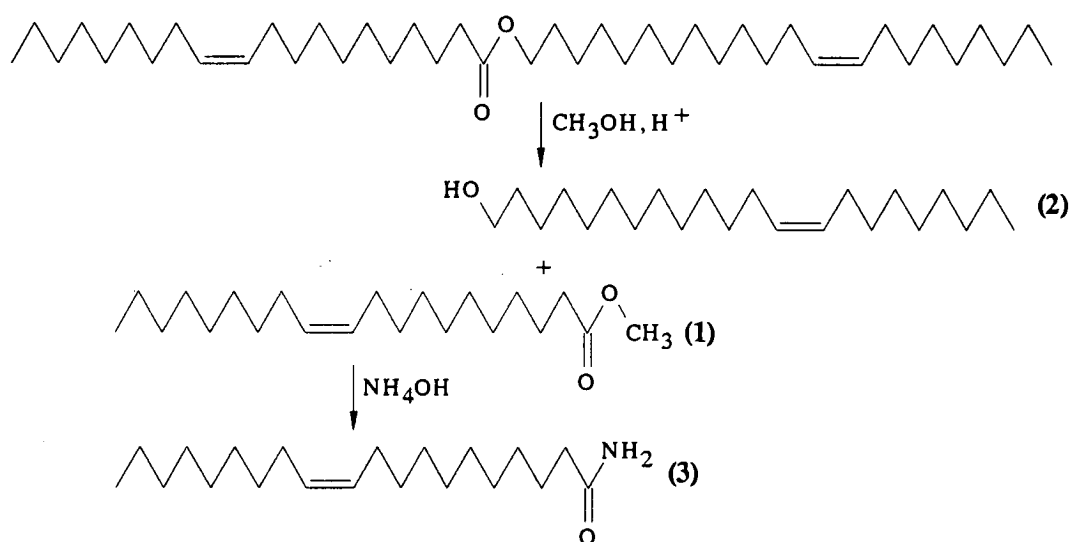


Scheme 38

As for reactions on the ester function, in the past, the Bouveault-Blanc reaction (reduction with sodium in ethanol) was an important and low cost route to unsaturated alcohols.<sup>127</sup> Acrylate and methacrylate esters have been synthesized from the alcohols and subsequently polymerised<sup>128</sup> under free radical conditions to form both homopolymers and copolymers. Infra-red spectroscopy showed that the vinyl region absorptions were absent but that the mid-chain isolated double bonds remained.

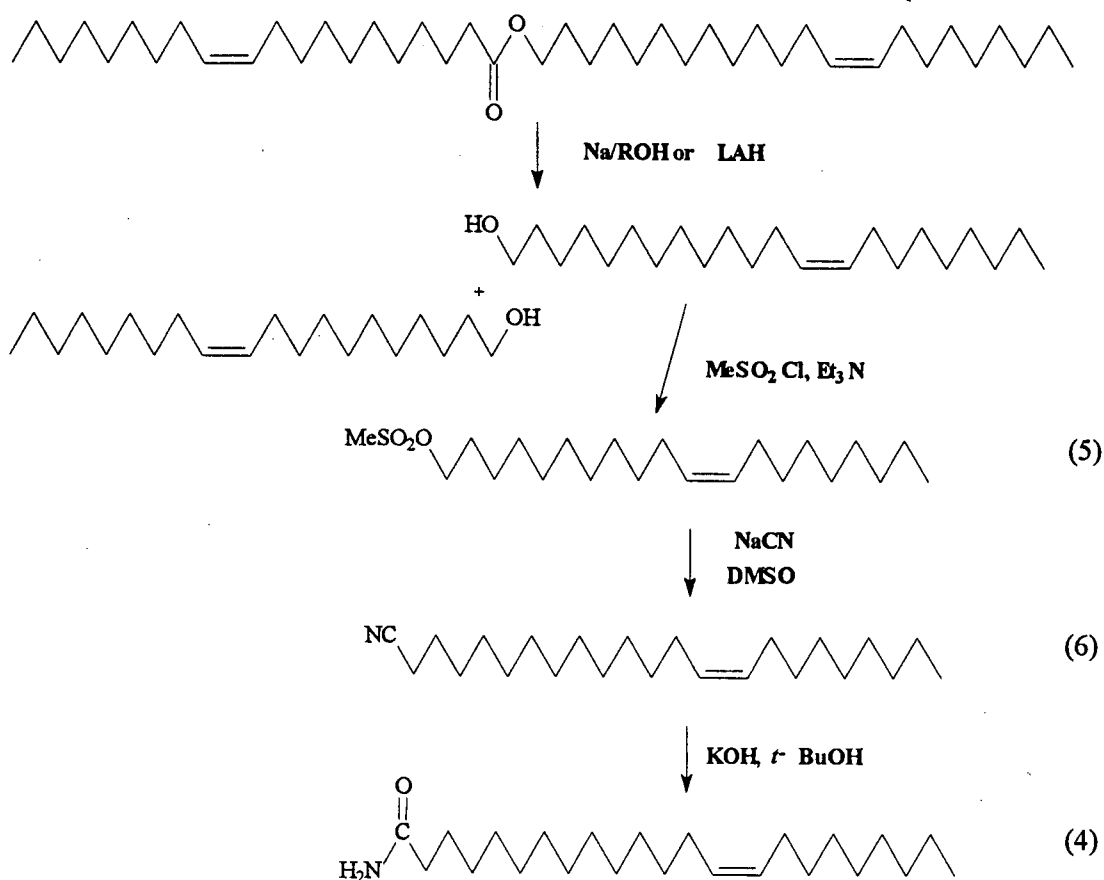
Primary fatty acid amides are known for their high surface activity, particularly as their presence in small quantities (<1%) can produce striking improvements when used as polymer additives, *eg.* they decrease the friction in polyethylene

film extrusion by over 50%.<sup>129</sup> The most straightforward synthesis of an amide from an ester is by the action of concentrated ammonium hydroxide, to form the solid amide. However, Shani *et al*<sup>130</sup> found this method unsatisfactory with jojoba oil (possibly because of steric interference and the oily nature of the ester). Instead they transesterified the oil to form methyl jojoboate (1) and jojoba alcohol (2) (Scheme 39). Conversion of this shorter chain ester to the amide (3) with aqueous ammonium hydroxide was then carried out.



Scheme 39

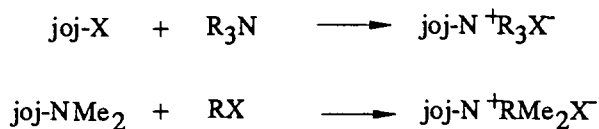
The higher homologue, homojojobamide (4), was also prepared by converting jojoba mesylate (5) into the nitrile (6), thus elongating the jojoba chain (Scheme 40). This nitrile was then hydrolysed to homojojobamide in high yield (70% from the oil).



**Scheme 40**

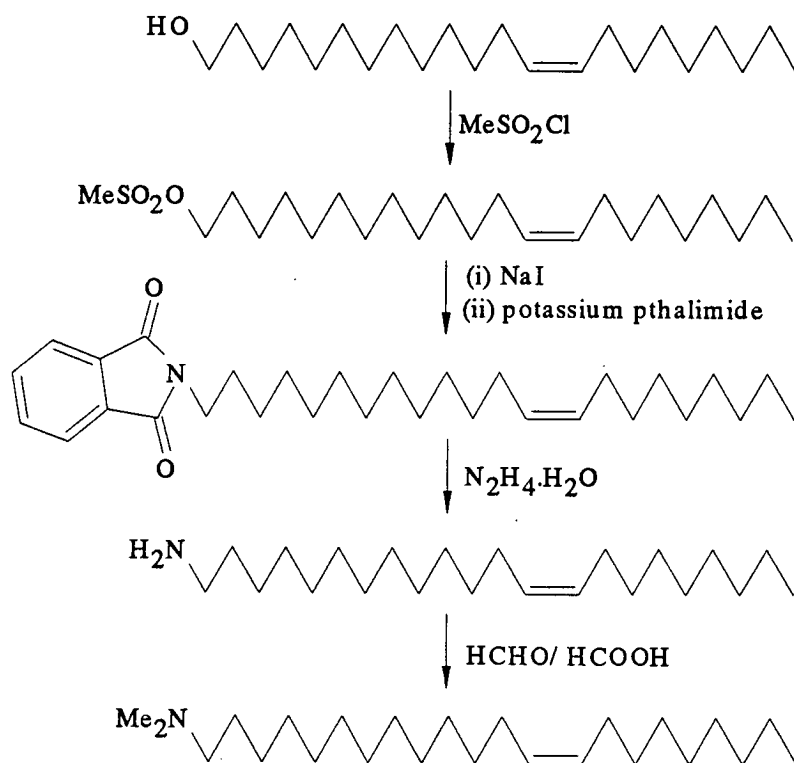
The surface activities of quaternary ammonium salts derived from jojoba have been measured;<sup>131</sup> and their presence found to reduce surface tension at very low concentrations. These salts may have potential as germicides, emulsifiers and phase transfer reagents. Their preparation, by two approaches, has been reported<sup>132</sup> (Scheme 41).

Firstly, by the reaction of a jojoba halide or mesylate (derived from the alcohol) with a tertiary amine. The second approach involves the preparation of dimethyljojobylamine (DMJA) and its reaction with alkyl halides.



**Scheme 41**

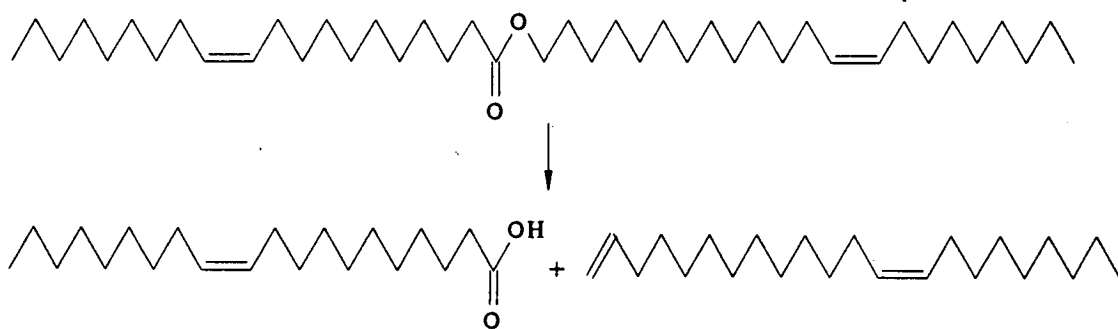
DMJA was synthesised from the alcohol portion of jojoba by the following reaction sequence: mesylation, iodination with sodium iodide, formation of an amine *via* the phthalimide and finally methylation (Scheme 42). A similar approach was used for the chain extended dimethylhomojojobylamines.



Scheme 42

Pyrolysis of jojoba oil at 375°C under reduced pressure and an atmosphere of nitrogen is reported<sup>119,133</sup> to produce a mixture of C<sub>18</sub>-C<sub>24</sub> unsaturated acids and dienes (Scheme 43). In the same paper, the dehydration of long chain jojoba alcohols was described using phosphoric acid or *p*-toluenesulfonic acid to produce dienes similar to those formed by pyrolysis.



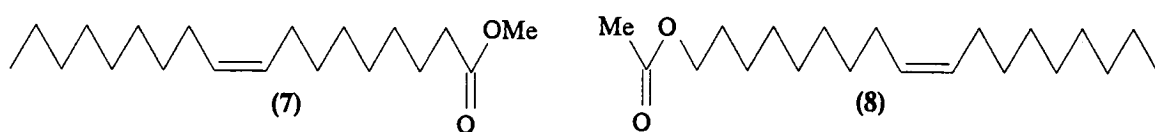


**Scheme 43**

Terminally unsaturated C<sub>12</sub> - C<sub>14</sub> fatty alcohols have been synthesised from jojoba oil by a process involving reductive cleavage of the oil, silylation of the C<sub>20</sub> - C<sub>22</sub> alcohols and metathesis of the silyl ethers with ethylene.<sup>140</sup> After cleavage of the silyl protecting group the alcohol yield was 70%.

## 2.2 Ene Additions to Jojoba Oil

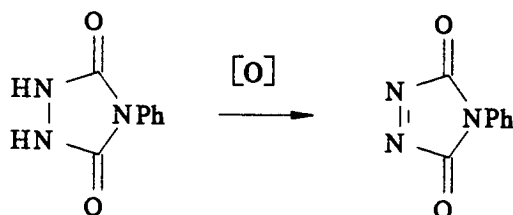
Before studying jojoba oil itself, methyl oleate (7) and oleyl acetate (8) were examined as monounsaturated models for the acid and alcohol fragments of the wax ester, respectively. Methyl elaidate, the *trans* isomer of (7), was also studied for comparison. In order to further simplify the analysis, the short chain *cis* and *trans* isomers of 3-hexene and 5-decene were also used as ene components. As a consequence of their symmetry it was anticipated that each of these alkenes would produce only one regioisomeric ene adduct.



### 2.2.1 4-Phenyl-1,2,4-triazoline-3,5-dione (PTAD) as Enophile

PTAD, MTAD and DEAD are all examples of azodicarbonyl compounds.<sup>135</sup> The presence of carbonyl functions on both sides of the N=N bond in such species increases the reactivity of the azo groups and they find wide use as dienophiles,<sup>136,137</sup> enophiles<sup>138</sup> and they can also act as electrophiles.<sup>139</sup> As dienophiles, azo compounds are generally more reactive than the corresponding alkene system as their lowest unoccupied molecular orbitals are of lower energy (and the reaction is controlled by the HOMO-diene LUMO-dienophile interaction). Constraint of the azo linkage into a ring lowers the LUMO energy still further. These energy arguments can be extended to explain the high reactivity as enophiles of triazolinediones, such as PTAD and MTAD. In fact, PTAD has been estimated to be at least 30000 times more reactive towards cyclohexene than DEAD.<sup>138</sup> Although many other 4-substituted derivatives appear in the literature, the 4-phenyl derivative is by far the most cited. It is readily synthesised by oxidation of 4-phenylurazole (Scheme 44) using, for example, *tert*-butyl hypochlorite,<sup>140</sup> lead

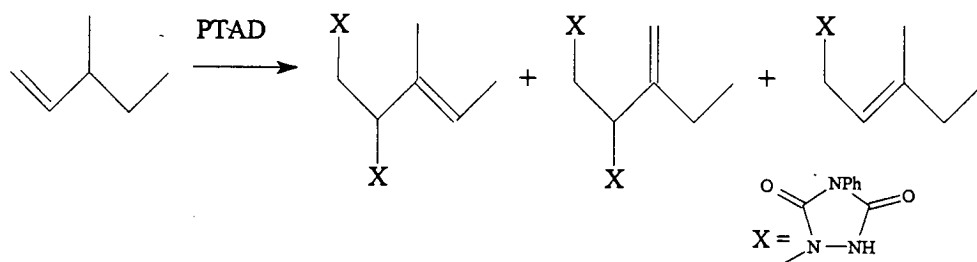
tetraacetate,<sup>141</sup> nitrogen dioxide,<sup>142</sup> lead dioxide,<sup>143</sup> *N*-bromosuccinimide,<sup>144</sup> *p*-toluenesulfonyl isocyanate in DMSO<sup>145</sup> and benzeneseleninic anhydride.<sup>146</sup>



**Scheme 44**

In the present work the oxidation step was carried out using NBS and the crude product sublimed to produce bright red, needle-like crystals in good yield (87%). PTAD is known to decompose under UV irradiation to nitrogen, carbon monoxide and phenyl isocyanate<sup>147</sup> and it also degrades slowly in methylene chloride. For these reasons it was stored in the dark at  $< -4^{\circ}\text{C}$ . Before use, its melting point was rechecked to ensure that the enophile had not decomposed.

Ohashi *et al*<sup>148</sup> have made a study of the addition of PTAD to a selection of simple alkenes as models for polyisoprene. They noted that for 3-methyl-1-pentene and 3-methyl-1-butene the initial ene adducts contained highly substituted double bonds which were more reactive than the original alkenes and underwent a second ene addition to form 2:1 adducts. Scheme 44a shows the products formed from reaction of PTAD with 3-methyl-1-pentene (for which the ratio of monoadduct to diadducts was 1:3). For straight chain alkenes, both terminal and 1,2-disubstituted, they noted no formation of diadducts with PTAD.

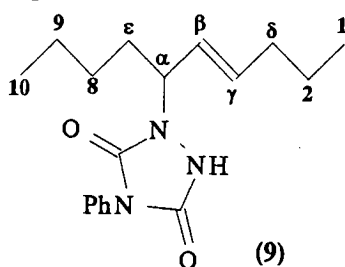


Scheme 44a

Further attempts by Ohashi and Butler<sup>149</sup> to form diadducts by reacting ene 1:1 adducts with PTAD yielded complex product mixtures with no evidence for simple 2:1 adducts. Their NMR spectra showed very broad peaks and it is thought that the PTAD may have reacted with the acidic NH hydrogen of the urazole ring. Only one *cis* alkene, *cis*-2-butene, was used in this work and so these systems were not ideal as models for jojoba or other vegetable oils which contain only *cis* unsaturation.

### 2.2.1.1 *cis* and *trans*-5-Decenes as Model Compounds

A slight excess (1.2 equivalents) of both *cis* and *trans*-5-decene was reacted with PTAD in a solution of methylene chloride at 0°C. Once the red colour of the PTAD had been discharged (in approximately 60 minutes), the solvent and excess unreacted decenes were removed under vacuum and the residues were recrystallised from cyclohexane. Both alkenes yielded white crystalline solids with superimposable  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra and whose melting points and mixed melting points were identical (70.7 - 72.0°C). From the NMR spectra the products from both reactions were assigned structure (9). In this and subsequent adducts, the central new alkene unit and adjacent atoms are labelled using the same Greek letters to facilitate comparisons between adducts of varying chain lengths.

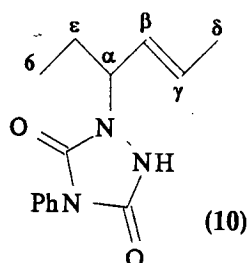


In addition to the anticipated signals for the urazole moiety, the products show distinctive NMR absorptions for the new alkene unit and the adjacent allylic positions. In order to fully assign these spectra, irradiation experiments were carried out and a  $^1\text{H}$  -  $^{13}\text{C}$  correlation spectrum was obtained to unambiguously identify the alkene ( $\beta$  and  $\gamma$ ), C( $\delta$ ) and C( $\epsilon$ ) signals. In the proton spectra, H( $\beta$ ) appears as a doublet of doublets of triplets at 5.43 ppm and H( $\gamma$ ) as a doublet of triplets of doublets at higher frequency (5.75 ppm). The 15.4 Hz coupling between these alkene protons confirms the assignment of *trans* geometry. The broad signal from the urazole NH appears at 9.55 ppm. Despite a careful search of  $^{13}\text{C}$  NMR spectra of the products and of the mother liquors, there was no evidence for the presence of *cis*-alkenes. Their allylic methylene signal would appear at *ca.* 27 ppm<sup>80</sup> for C( $\delta$ ) and doubling

elsewhere would be expected, especially for C( $\alpha$ ) and C(2). There are characteristic peaks for the allylic CHN [H( $\alpha$ ) 4.58 ppm, C( $\alpha$ ) 58.50 ppm] and allylic methylene [H( $\delta$ ) 1.97 ppm, C( $\delta$ ) 34.16 ppm]. At 360 MHz the protons of the methylene adjacent to the allylic CHN (CH<sub>2</sub>- $\epsilon$ ) appear as a pair of diastereomeric signals centred at 1.66 ppm. There was no evidence of further PTAD addition to the new *trans*-alkene unit in the product to form a diadduct. This observation is in accord with the research of Ohashi *et al*<sup>148</sup> who found only mono-adducts on addition of PTAD to terminal and 1,2-disubstituted alkenes.

### 2.2.1.2 *cis* and *trans*-3-Hexenes as Model Compounds

The shorter chain, *cis* and *trans*-3-hexenes reacted similarly (in 35 minutes) to form a white crystalline solid which melted at 102 - 103°C after recrystallisation from cyclohexane. The product was identified from its analytical and spectroscopic data as ene adduct (10).

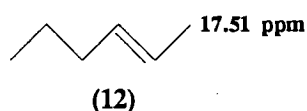
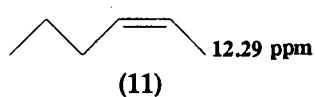


Selected <sup>1</sup>H and <sup>13</sup>C NMR data for the hexene and decene adducts (10 and 9) is shown in Table 1.

Table 1

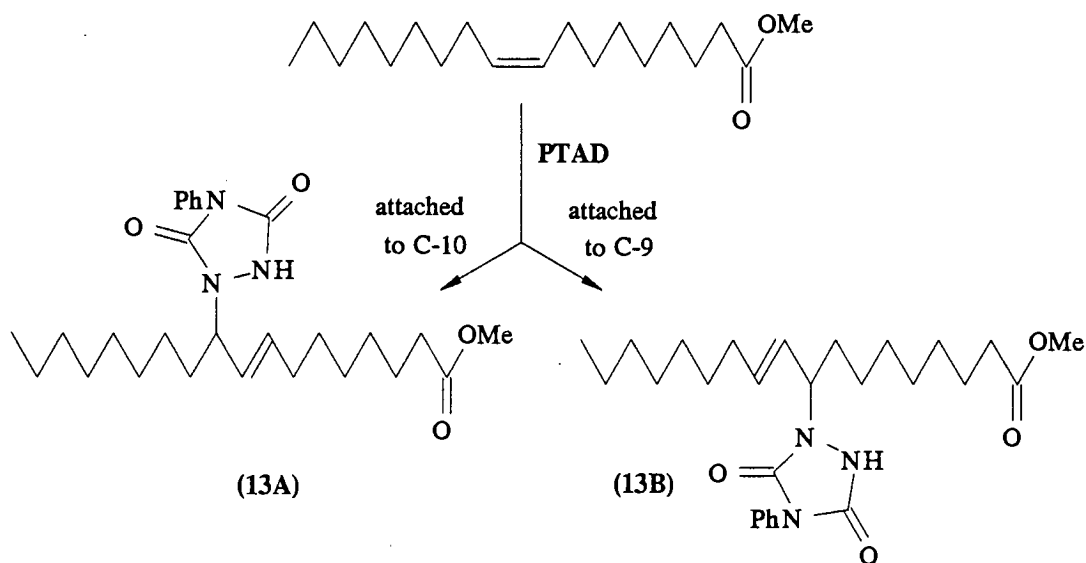
Selected $^1\text{H}$ and $^{13}\text{C}$ NMR data for ene adducts (10 and 9)								
Starting alkene (adduct)	$\delta_{\text{H}}/\text{ppm}$				$\delta_{\text{C}}/\text{ppm}$			
	$\alpha$	$\beta$	$\gamma$	$\delta$	$\alpha$	$\beta$	$\gamma$	$\delta$
(Z)-3-hexene (10)	4.47 q	5.42 ddq	5.74 dq	1.64 dd	59.87	126.74	130.40	17.52
(Z)-5-decene (9)	4.58 q	5.43 ddt	5.75 dtd	1.97 q	58.50	125.88	135.62	34.18

The influence of the allylic methyl in (10) caused  $\text{C}(\gamma)$  to appear at lower frequency (130.40 ppm) compared to the decene adduct, while  $\text{C}(\beta)$  was slightly higher at 126.74 ppm. These differences were less marked in the  $^1\text{H}$  NMR. The coupling between the alkene protons of 15.4 Hz again confirmed that the geometry was *trans*. By comparison with the  $^{13}\text{C}$  NMR data for *cis* and *trans*-2-hexene (11 and 12), the absence of any *cis* adduct was further confirmed as the allylic methyl signals ( $\text{C}-\delta$  in the product) appeared at 17.52 ppm (*ie.* at an almost identical frequency to the terminal methyl in *trans*-2-hexene) and furthermore there was no absorbance in the 12.3 ppm region of the spectrum (of compound 10) which would be expected if the adduct contained any *cis* unsaturation.



### 2.2.1.3 Methyl Oleate and Methyl Elaidate as Model Compounds

From the decene and hexene studies it was predicted that methyl oleate and methyl elaidate (the *cis* and *trans* isomers of methyl 9-octadecenoate) would undergo ene additions to give identical products with *trans* geometry, although as the ene component is not symmetrically substituted, two regioisomers would be formed (13A & 13B) depending whether the enophile becomes attached at the C-10 or C-9 alkene position (Scheme 45).



Scheme 45

The reactions were carried out by stirring equimolar quantities of the alkenes with PTAD in dichloromethane at 0°C. After removal of the solvent, chromatography afforded unreacted alkene followed by the ene adducts. The yields were excellent: 92% and 94% for methyl oleate and elaidate respectively. The recovered alkene from the methyl oleate experiment was examined by  $^{13}\text{C}$  NMR for isomerisation to the thermodynamically more stable *trans* geometry. There was no evidence for the *trans* allylic carbon signal at 32.5 ppm and the *cis* allylic methylene signal remained strong at 27.1 ppm in the recovered alkene. Neither were any changes observed in the recovered methyl elaidate spectra. It is therefore concluded that formation of



the *trans* double bond in the adducts occurs during the ene addition rather than by isomerisation of the starting alkene followed by the addition step.

The NMR spectra for the two ene products were identical and the characteristic peaks for the new alkene unit are presented in Table 2 for comparison with the signals for the model adduct derived from the 5-decenes (9). Full NMR assignments are tabulated in Appendices 1 and 2.

Table 2

Selected <sup>1</sup> H and <sup>13</sup> C NMR data for ene adducts 9, 13 and 14								
Starting alkene (adduct)	$\delta_H$ /ppm				$\delta_C$ /ppm			
	$\alpha$	$\beta$	$\gamma$	$\delta$	$\alpha$	$\beta$	$\gamma$	$\delta$
(Z)-5-decene (9)	4.58 q	5.43 ddt	5.75 dtd	1.97 q	58.50	125.88	135.62	34.18
methyl oleate (13)	4.53 q	5.40 dd	5.71 dtd	1.95 q	58.49 58.51	125.61 125.82	135.44 135.77	ca. 31.8
oleyl acetate (14)	4.54 q	5.40 dd	5.72 dt	1.96 q	58.49	125.60 127.77	135.52 135.77	31.75 32.00

It is evident from Table 2 that 5-decene was a good model to aid spectral assignment in the more complex unsaturated ester. The C- $\delta$  signal in the decene-derived adduct is, however, at a conspicuously higher frequency than the oleate adduct. This is easily rationalised because the carbon signal at  $\omega$ -2 (where  $\omega$  is a chain terminus) is often shifted to higher frequency than that for a typical mid-chain methylene. This is known as the "gamma-gauche effect"<sup>150</sup> and in this case it is affecting C( $\delta$ ) in the decene adduct.

Doubling of the signals for carbons  $\alpha$ ,  $\beta$ ,  $\gamma$  and  $\delta$  is attributed to the presence of regioisomers (13A&B). The fact that the doubled peaks are of equal intensity indicates that the enophile does not show a preference for adding at either C-9 or C-10 but forms both regioisomers in equal quantities.

#### 2.2.1.4 Kinetic Studies on Model Compounds

It was noted that while methyl oleate decolourised an equimolar quantity of PTAD in 40 minutes, the equivalent reaction with methyl elaidate was much slower, taking 2.5 hours to reach completion. This is in accord with earlier observations by Cheng *et al*<sup>14</sup> who found that in the reactions of *cis* and *trans* 3-hexenes with PTAD (at 23°C in dichloromethane) the *cis* isomer reacted 5.9 times faster than the *trans*, while for the 2-butenes, the *cis* isomer was again 2.1 times more reactive. They proposed a parallel planes approach of ene and enophile (Figure 4) and noted that, in three-centre olefin-electrophile reactions, *cis* alkenes are commonly more reactive than *trans* (while the *trans* isomer reacts faster in addition reactions proceeding *via* 4, 5 and 6 membered cyclic activated complexes).<sup>151</sup>

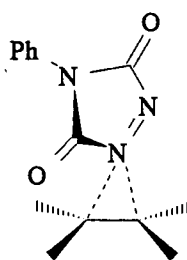
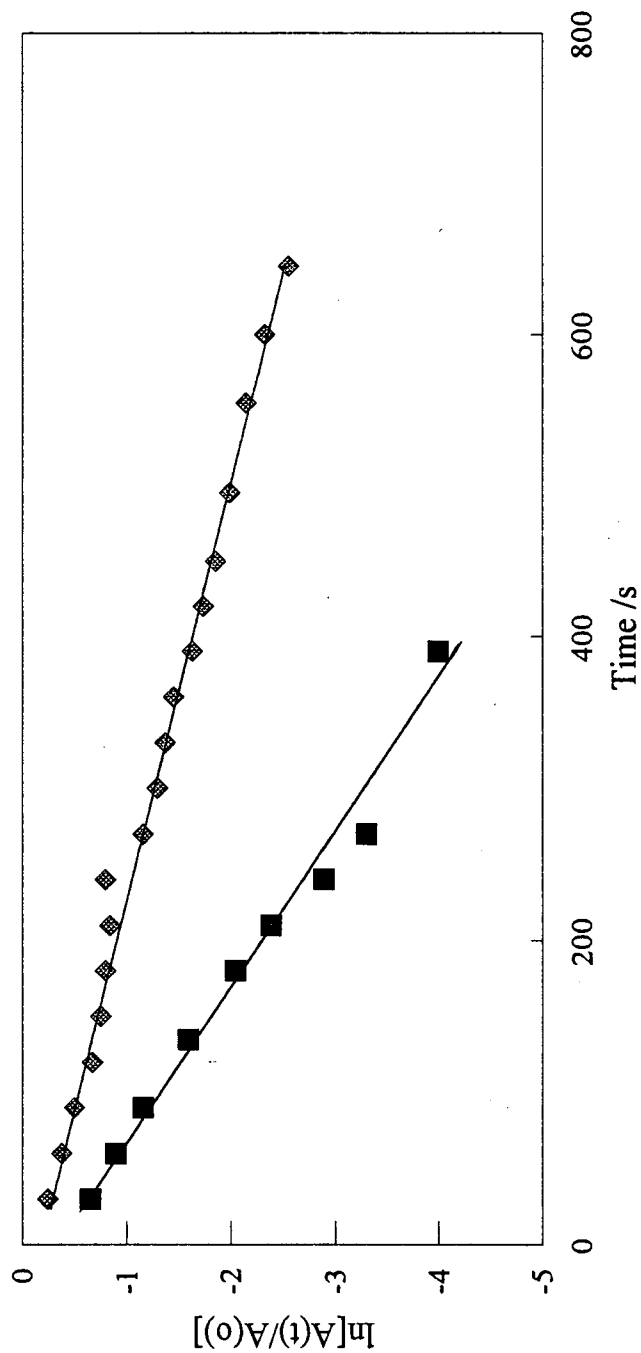


Figure 4

Kinetics by UV/Visible Monitoring  
PTAD Consumption with Methyl Oleate and Elaidate



Graph 1

Kinetic experiments were carried out on the present system in order to quantify the differing reaction rates of methyl oleate and methyl elaidate. The consumption of the PTAD was measured spectrophotometrically under pseudo first order conditions (*ie.* with a ten times excess of the alkene) over four half-lives using UV/visible monitoring. Plotting the logarithm of [the absorbance at time,  $t$ , divided by the initial absorbance] against time gave a straight line (Graph 1) whose gradient gave the pseudo first order rate constant ( $k_1'$ ). On dividing this figure by the initial concentration of the excess alkene, a value for the second order rate constant for the reaction was obtained. It was calculated that at 21°C PTAD reacted with methyl oleate 2.75 times faster than with methyl elaidate ( $k_2 = 1.08$  and  $0.40 \text{ mol}^{-1}\text{dm}^3\text{s}^{-1}$  respectively).

In Table 3 the second order rate constants found for methyl oleate and elaidate are compared with related values found by Cheng *et al*<sup>14</sup> for *cis* and *trans* 3-hexenes and 2-butenes. It is concluded that the combination of steric and electronic effects caused by changing the alkyl substituents on the double bond has a marked effect on the relative reactivities of the ene components.

Table 3

Alkene	Temp /°C	Second order rate constants ( $k_2 \times 10^2$ )/ $\text{mol}^{-1}\text{dm}^3\text{s}^{-1}$		Ratio $k_{2cis}:k_{2trans}$
		<i>cis</i>	<i>trans</i>	
3-hexene <sup>a</sup>	23.5	89	15	5.9:1
methyl oleate & methyl elaidate	21	108	40	2.75:1
2-butene <sup>a</sup>	23.5	38	18	2.1:1

<sup>a</sup> results from Cheng *et al*<sup>14</sup>

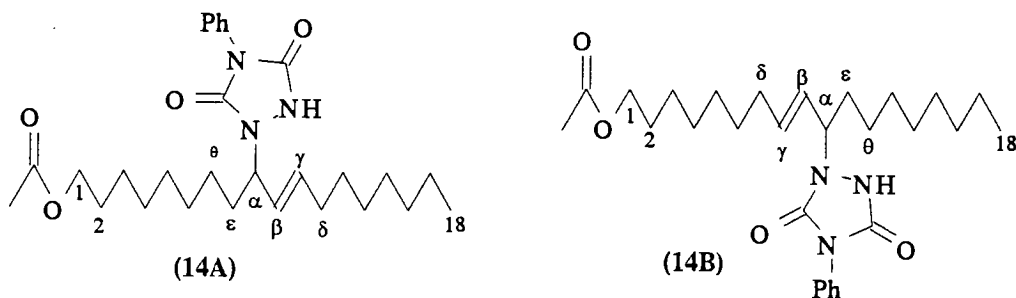
An alternative measurement was attempted, still under pseudo first order conditions with the PTAD in excess, but this time monitoring the



disappearance of the alkenes by capillary gas chromatography. This approach, however, was unsuccessful as with the PTAD in such excess the reaction was too fast to measure, all the alkene being consumed within one minute of mixing.

### 2.2.1.5 Oleyl Acetate as a Model Compound

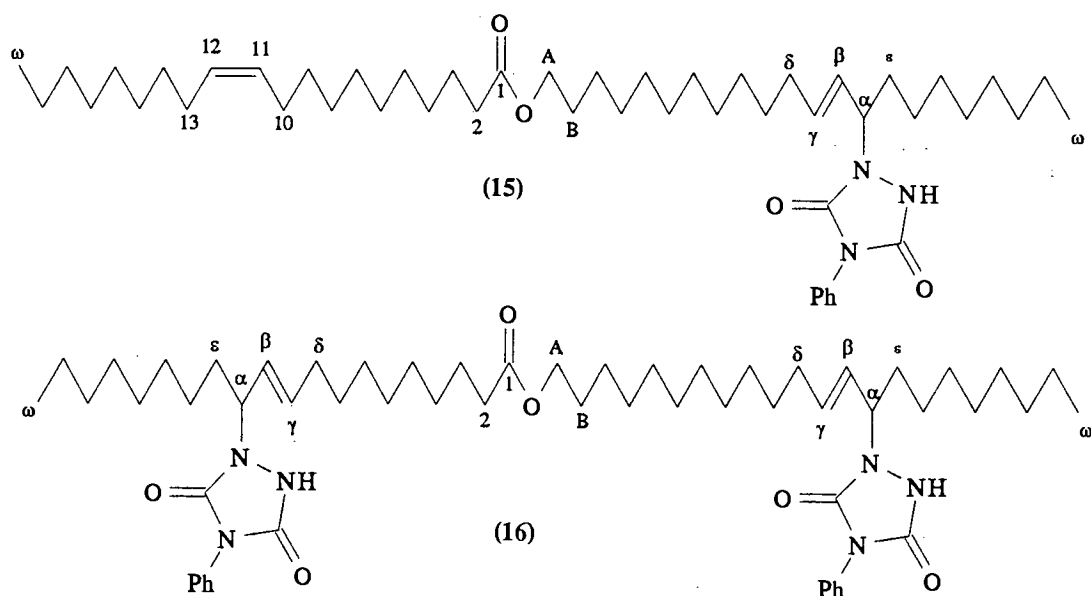
Oleyl acetate was examined as a model for the unsaturation present in the alcohol portion of jojoba oil. Treatment with PTAD yielded ene adducts which were characterised by their  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra as 14A and 14B in a combined yield of 90%.



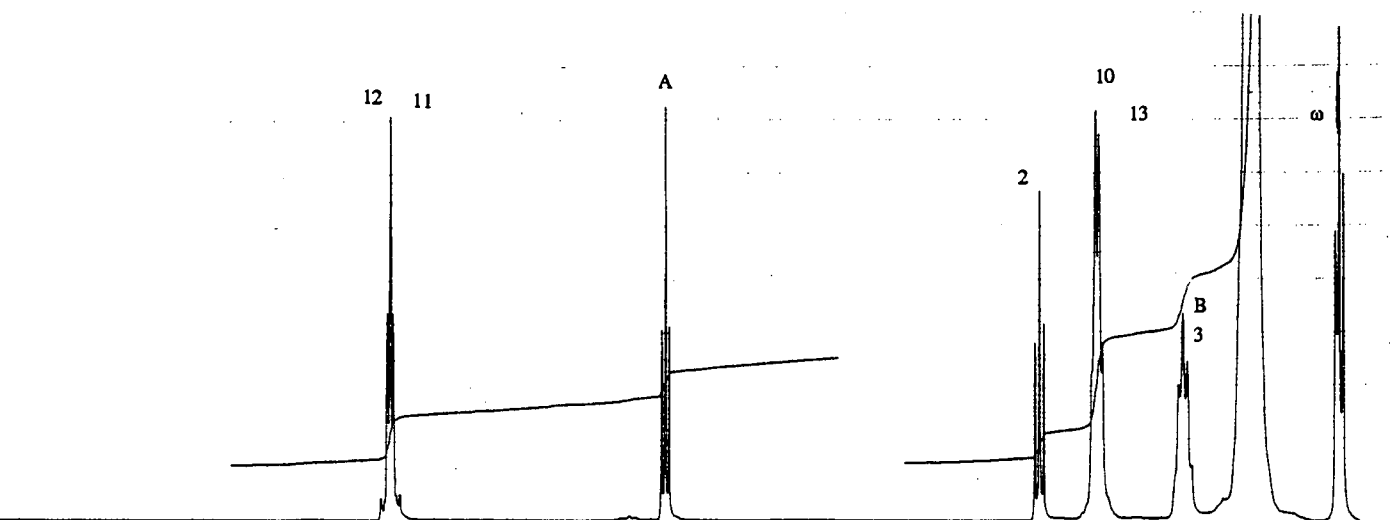
As anticipated, the new alkene unit and associated allylic signals in the NMR spectra were indistinguishable from those of the methyl oleate and methyl elaidate derived analogues. Table 2 shows the NMR data for comparison. The only significant differences in the spectra are caused by the presence of the acetate group which shifts the proton and carbon signals of the adjacent methylenes in the chain to higher frequencies. Proton and  $^{13}\text{C}$  NMR assignments are tabulated in Appendix 3.

### 2.2.1.6 Modification of Jojoba

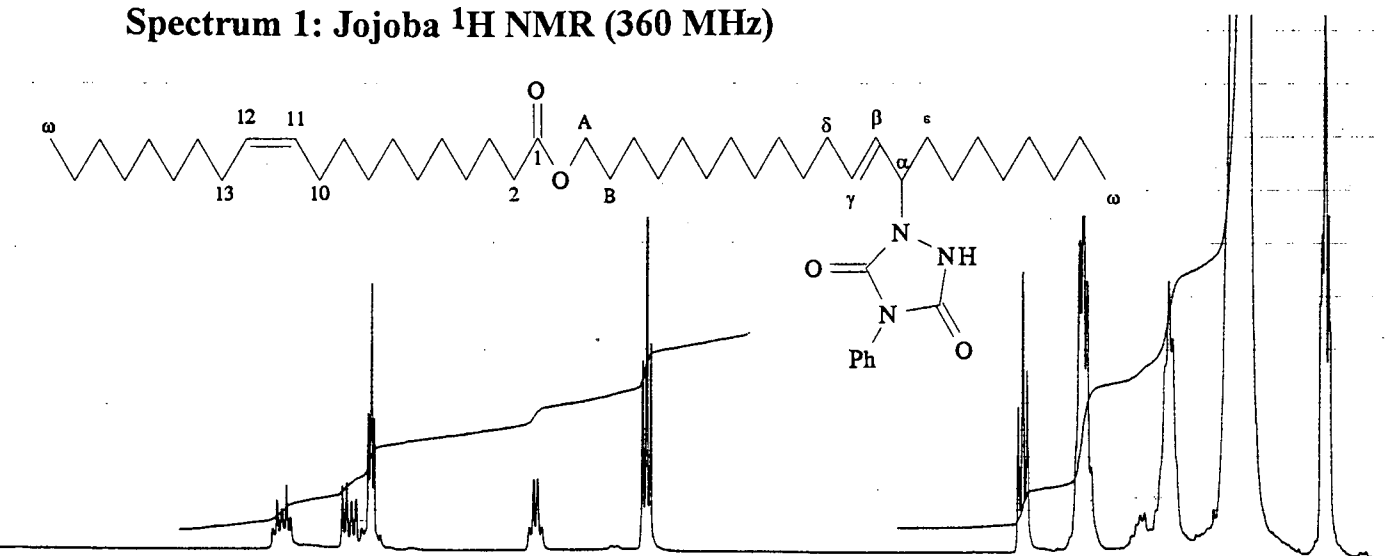
Having established that PTAD adds readily to typical monounsaturated lipids in high yields, the corresponding reaction with jojoba oil was investigated. Treatment of jojoba oil with PTAD in dichloromethane at 0°C afforded, after removal of the solvent, a yellow oil. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of the crude product showed the presence of both ene adduct and unreacted lipid alkenes. By comparing the intensities of the ester  $\text{OCH}_2$  and allylic  $\alpha\text{-CHN}$  signals at 4.04 and 4.56 ppm it was estimated that 29% of the double bonds had reacted. Chromatography of the reaction mixture afforded, in order of elution: unreacted jojoba oil (41%), a fraction composed of 1:1 adducts (36%) and finally a mixture of 2:1 adducts (15%). Compounds (15) and (16) are representative of the 1:1 and 2:1 adducts and their NMR spectral assignments are fully characterised in Appendices 4 and 5.



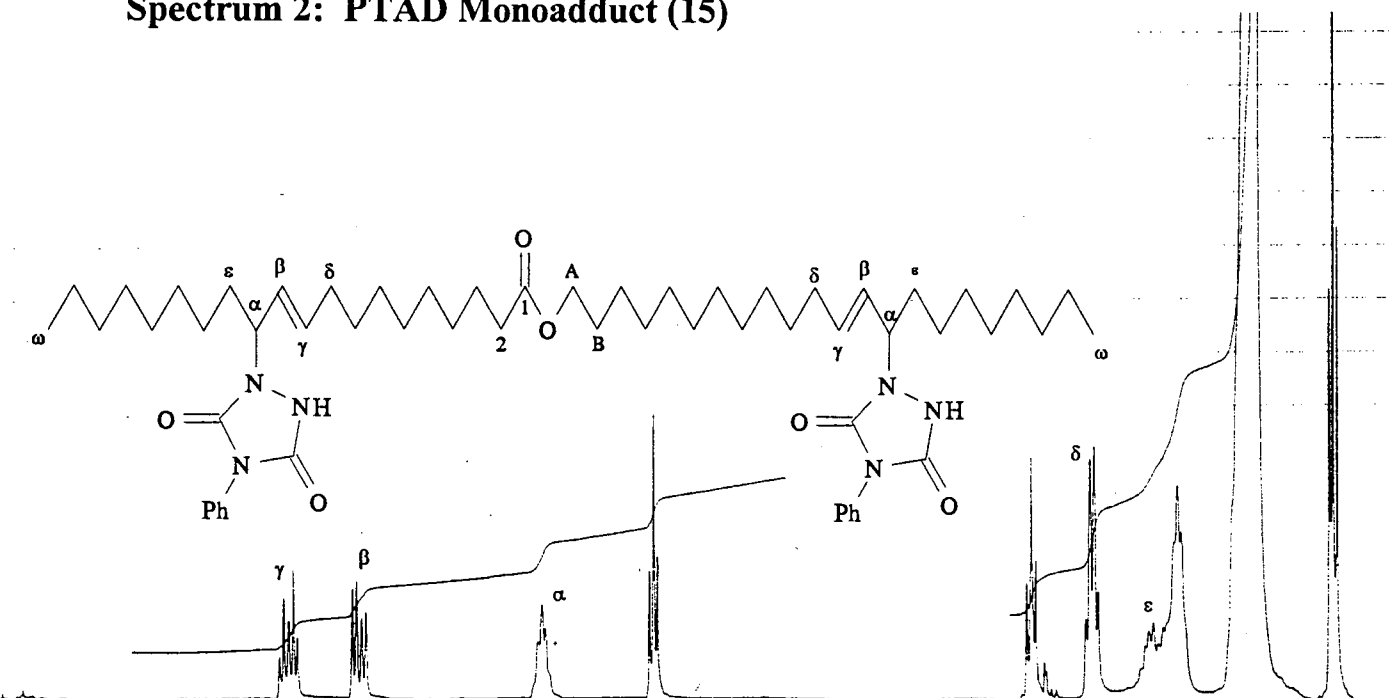
The  $^1\text{H}$  NMR spectra of jojoba oil and its 1:1 and 2:1 adducts (15 & 16) with PTAD are shown in spectra 1, 2 & 3. In the progression from spectrum 1 to 2 to 3, the jojoba alkene proton signal at 5.32 ppm reduces in size until, in spectrum 3, it has disappeared. At the same time the signals for the new alkene protons in the adducts (at 5.42 and 5.73 ppm) increase in intensity with



**Spectrum 1: Jojoba  $^1\text{H}$  NMR (360 MHz)**



**Spectrum 2: PTAD Monoadduct (15)**



**Spectrum 3: PTAD Diadduct (16)**

respect to the lipid (as estimated by comparison with the signal at 4.04 ppm from the methylene adjacent to the ester function). In Spectrum 2 the integrals of the new alkene unit *versus* those of the unreacted jojoba proton are equivalent which indicates that each molecule has one modified double bond and one unmodified double bond. In contrast, the integral ratios in Spectrum 3 of the new alkene signals *versus* the total lipid OCH<sub>2</sub> is 2:1 which confirms that both double bonds have been modified. As jojoba oil itself is composed of a mixture of chain lengths, the signals in the <sup>13</sup>C NMR are intrinsically broader than those for the model compounds (13A&B and 14A&B) and the doubling of peaks is no longer visible. It is presumed that regioisomers are still being formed by analogy with the model adducts. The recovered jojoba oil was examined by <sup>13</sup>C NMR for evidence of isomerisation to *trans* jojoba and was found to be unchanged.

#### 2.2.1.7 Kinetic Studies on Jojoba Oil

The rate of consumption of PTAD by jojoba was monitored by UV/visible spectroscopy, as described in Section 2.2.1.4 for methyl oleate and elaidate. A comparison of the reaction rates of jojoba and *trans*-jojoba with the oleate and elaidate models is shown in Graph 2. The jojoba rates are *ca.* twice as fast as there are two double bonds per molecule which can take part in the reaction. The second order rate constants were calculated to be:

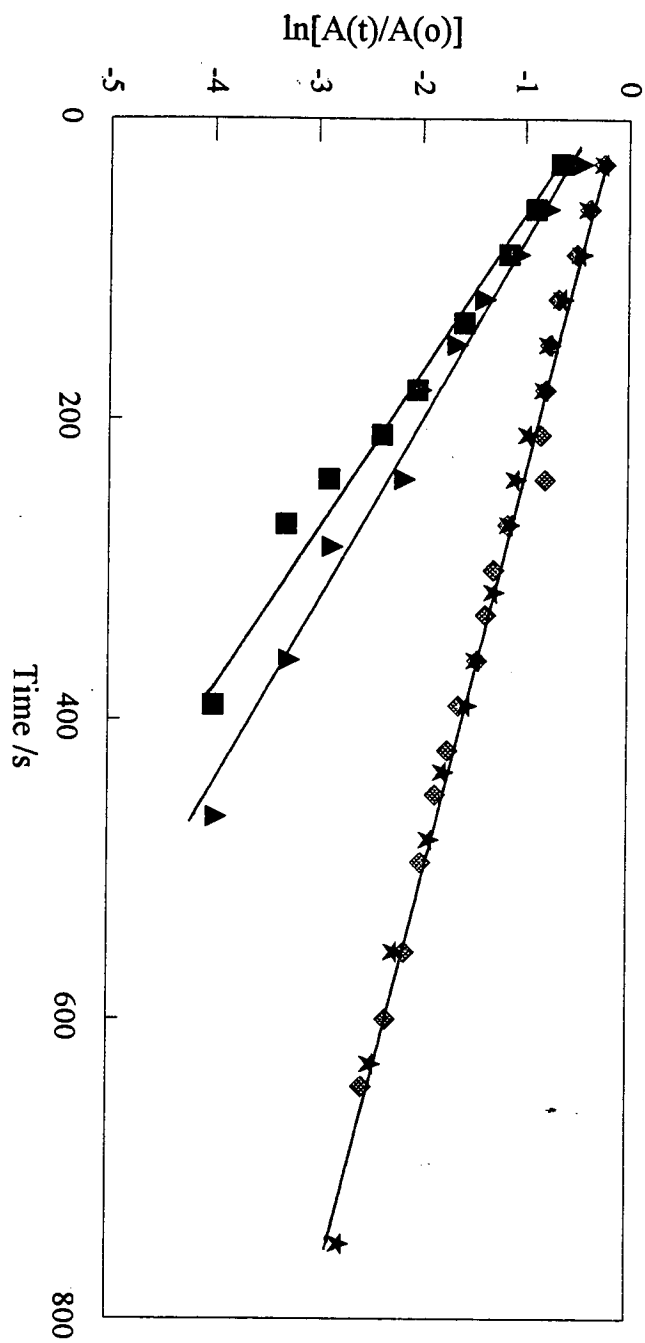
$$\begin{array}{ll} \text{methyl oleate} = 1.1 \text{ M}^{-1}\text{s}^{-1} & \text{jojoba} = 1.9 \text{ M}^{-1}\text{s}^{-1} \\ \text{methyl elaidate} = 0.40 \text{ M}^{-1}\text{s}^{-1} & \text{trans-jojoba} = 0.83 \text{ M}^{-1}\text{s}^{-1} \end{array}$$

These rate constants confirm that the methyl esters chosen were suitable models for jojoba. The graph on the following page shows the absorbances of jojoba and *trans*-jojoba divided by two, in order to account for the presence of two double bonds per molecule in comparison with the models.



# Kinetics by UV/Visible Monitoring

PTAD Consumption with Methyl Oleate, Elaidate, Jojoba and trans-Jojoba



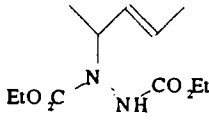
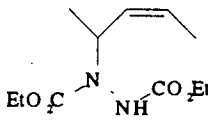
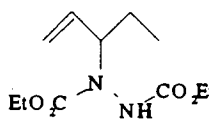
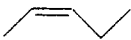

Graph 2

- Methyl Oleate
- ◆ Methyl Elaidate
- ▲ Jojoba Oil
- ★ Trans-Jojoba Oil

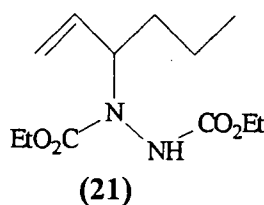
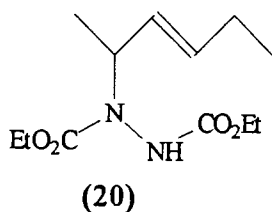
### 2.2.2 Diethyl Azodicarboxylate (DEAD) as Enophile

Researchers in the past have described the addition of DEAD to simple non-terminal alkenes. For both *cis* and *trans*-2-pentenes Thaler and Franzus<sup>152</sup> observed three product peaks by GC. In both cases the major product was assigned as the *trans*-4-substituted-2-pentene (17) while differing amounts of the *cis* isomer (18) were formed. The proportions of the 3-substituted-1-pentene (19) adduct also varied depending on the geometry of the ene component (Table 4).

Table 4

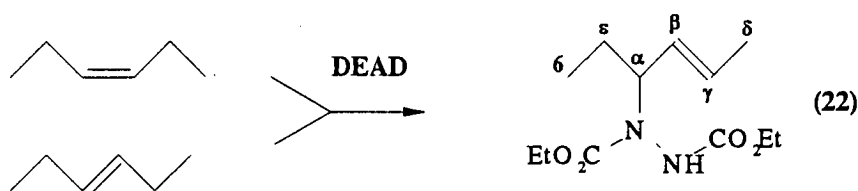
Starting 2-pentenes	Product Distributions of (17, 18 & 19) /%		
	 (17)	 (18)	 (19)
	65%	16%	19%
	62%	8%	30%

In contrast, on addition of DEAD to *trans*-2-hexene, Shah and George<sup>153</sup> did not report the presence of any *cis* isomeric product but observed only two peaks by GC, which they assigned to the mid-chain and terminally unsaturated adducts (20 and 21) (85:15, 74% yield).



### 2.2.2.1 *cis* and *trans*-3-Hexenes as Model Compounds

DEAD is a less reactive enophile than PTAD (Section 2.2.1) and the additions were therefore carried out in refluxing 1,1,1-trichloroethane (77°C) or 1,2-dichloroethane (83°C). Once again the symmetrical model alkenes *cis* and *trans*-3-hexenes reacted to furnish the same ene adduct which was isolated in each case by dry flash chromatography and identified as compound (22) from its NMR spectra (Scheme 46).

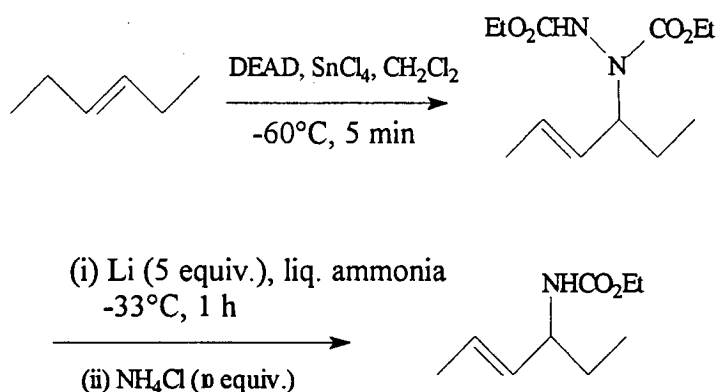


Scheme 46

The vinyl protons have similar spectral characteristics to those in the corresponding PTAD adduct. The <sup>1</sup>H NMR contains a doublet of doublets of multiplets at 5.34 ppm and a doublet of quartets at 5.57 ppm for β-H and γ-H (with a large mutual coupling of 15.4 Hz indicating *trans* geometry) while the corresponding carbon signals are found at 128.11 and 128.68 ppm. The allylic methyl group signal further confirms that the adduct has *trans* geometry as C-δ appears at 17.59 ppm (in contrast to a *cis* allylic methyl which would be expected at *ca.* 12.3 ppm). The allylic CH which becomes attached to the nitrogen of DEAD is visible at 4.36 ppm in the proton spectrum; but is concealed in the carbon spectrum by the strong CH<sub>2</sub> signals of the two ethyl ester groups from the enophile. Additional evidence that both the starting alkenes led to the same adduct was found by carrying out a <sup>1</sup>H NMR spiking experiment.

TLC of the crude reaction mixture revealed small quantities of more polar material but this was not identified. The possibility of some diadduct

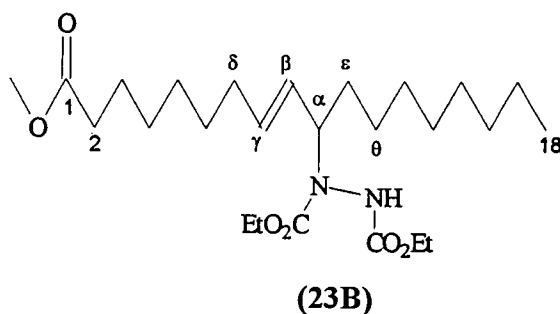
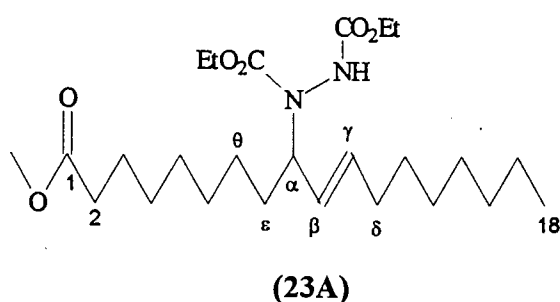
formation in these additions cannot be excluded as the DEAD could perform a further ene addition to the new double bond in the mono-adduct. There is precedent for this: Thaler and Franzus<sup>152</sup> noted diadduct formation in up to 25% yield in the reaction of butenes with DEAD. Furthermore, in a recent communication on the Lewis acid mediated ene reaction of DEAD to alkenes, Brimble and Heathcock<sup>33</sup> commented that the thermal reaction is "plagued" by the formation of diadducts. They used one equivalent of tin tetrachloride to catalyse the additions to simple alkenes before reducing the adduct by cleaving the N-N bond using lithium in liquid ammonia to effect allylic amination. Under these conditions *trans*-3-hexene reacted to form the ene adduct in 95% yield (with exclusively *trans* geometry) before formation of the carbamate (76%) as illustrated in Scheme 47. This method has only been demonstrated so far with terminal alkenes that can form only one regioisomeric adduct.



Scheme 47

### 2.2.2.2 Methyl Oleate and Methyl Elaidate as Model Compounds

The lipid esters, methyl oleate and elaidate, were reacted in refluxing 1,2-dichloroethane and the products isolated by dry flash chromatography. After examination by  $^1\text{H}$  and  $^{13}\text{C}$  NMR the major products were identified, for both alkenes, as (23A & B) in yields of 60% and 71% respectively. Spectral analyses confirmed that the alkene proton signals showed the characteristic doublet of doublets for H( $\beta$ ) and doublet of triplets for H( $\gamma$ ) with a large mutual coupling of 15.0 Hz indicating *trans* geometry. The signals for carbons ( $\beta, \gamma, \delta, \theta$ ) appear doubled, an affect attributed to the presence of regioisomers (23A & B). A full assignment of the  $^1\text{H}$  and  $^{13}\text{C}$  NMR is given in Appendix 10.



The unreacted lipids were also isolated and found to be unisomerised by  $^1\text{H}$  NMR examination of the alkene region. A more polar component which accounted for 11 - 16% of the total lipid was also isolated from both reaction mixtures. Its examination by  $^{13}\text{C}$  NMR revealed four C=O absorptions, the alkene region contained two widely separated signals (123.2 and 137.5 ppm), two peaks were clearly visible at 57.6 and 60.2 ppm, and the DEAD-ester signals were stronger relative to the mono-adducts. This product was tentatively assigned as diadducts formed by the reaction of a second molecule of DEAD with the monoadducts.

### 2.2.2.3 Kinetic Studies on Model Compounds

It was noted that when DEAD was the enophile its colour faded faster with methyl elaidate than with methyl oleate. This is in contrast to the reactions with PTAD. Kinetic studies were carried out by two approaches: firstly, using UV/visible spectroscopy at 350-500 nm to measure the disappearance of the enophile (using a ten times excess of the alkenes), and secondly using capillary GC to monitor the competitive disappearance of the alkenes (with the enophile in ten times excess). These reactions were followed over 28 and 31 hours respectively and samples taken at regular intervals. The higher reactivity of methyl elaidate is illustrated in the UV absorption traces in Figure 5. The DEAD intensity at 400 nm reduces at a faster rate than in its reaction with methyl oleate.

UV/Visible Spectroscopy Traces of DEAD in Reaction with  
(i) methyl oleate and (ii) methyl elaidate

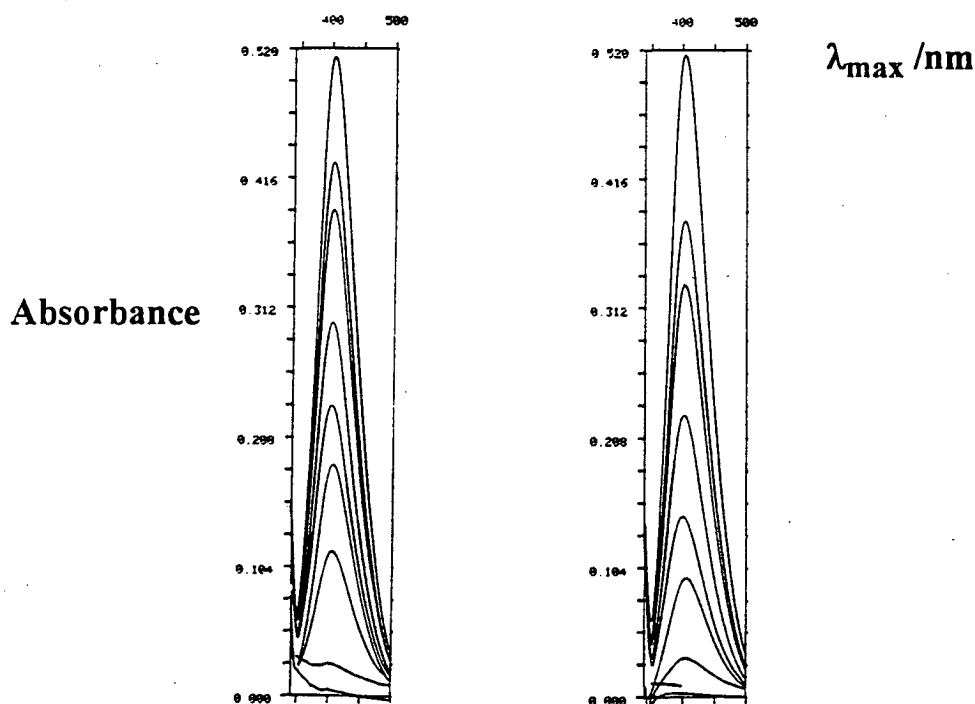


Figure 5

Graphs were plotted (as in 2.2.1.4) to find the pseudo first order rate constants, and from them the second order rate constants were calculated; these are shown in Table 5. The two sets of data cannot be directly compared as the reaction temperatures are different for each method. In both cases, however, DEAD reacts faster with the *trans* alkene and at higher temperatures the reaction proceeds more quickly with both ene substrates.

Table 5

Method of Monitoring	Solvent	Reflux Temp.	Second order rate constant, $k_2 \times 10^{-5} / \text{mol}^{-1} \text{dm}^3 \text{s}^{-1}$	
			methyl oleate	methyl elaidate
GC	1,1,1-trichloroethane	75°C	6.9	14.5
UV/visible	1,2-dichloroethane	83°C	7.6	17.2

These measurements are in accord with an earlier study by Thaler and Franzus<sup>152</sup> who noted that *trans*-2-butene reacted 3.7 times faster with DEAD than *cis*-2-butene. Their rationale was that *cis* alkenes have an unfavourable steric interaction between an alkyl substituent and one of the carbonyl groups on the enophile which does not occur with *trans* alkene geometry. This is sketched in Figure 6.

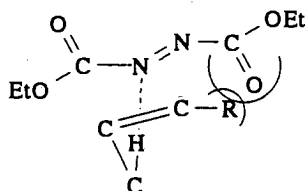
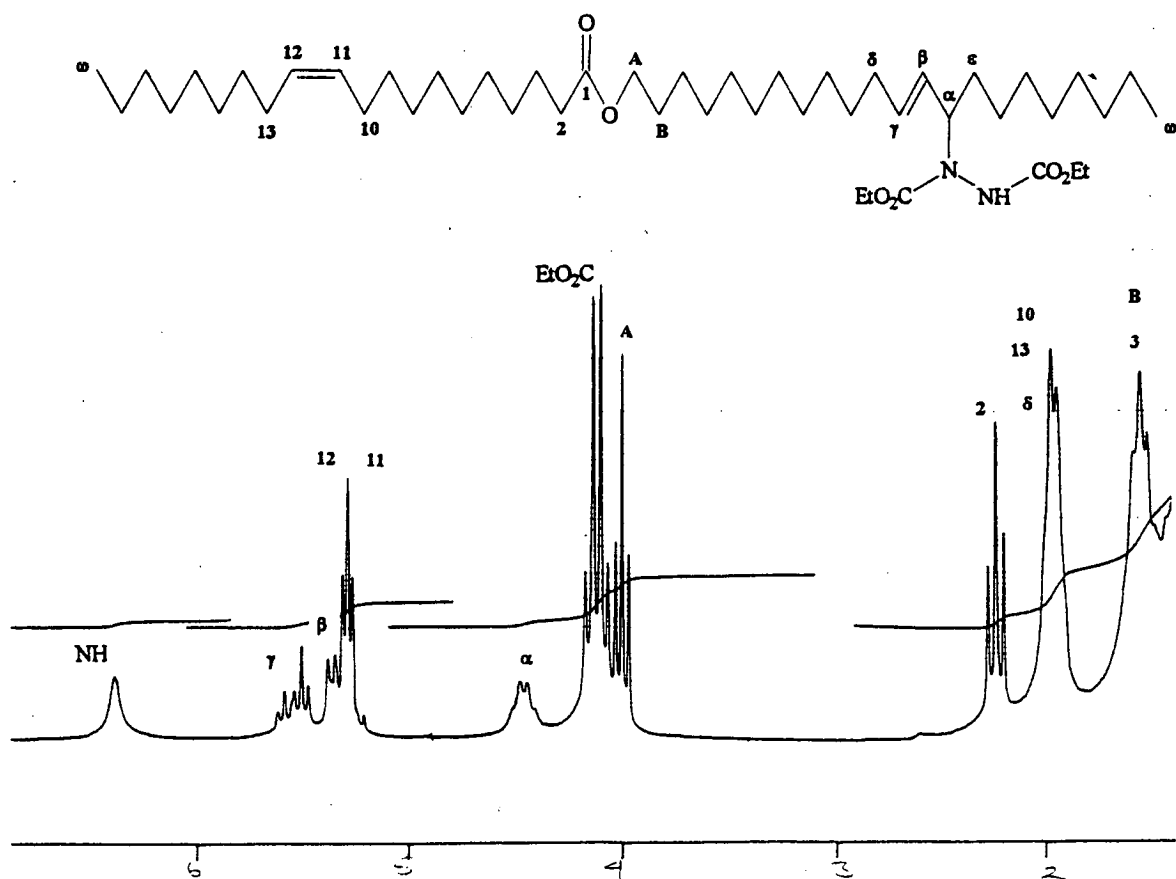
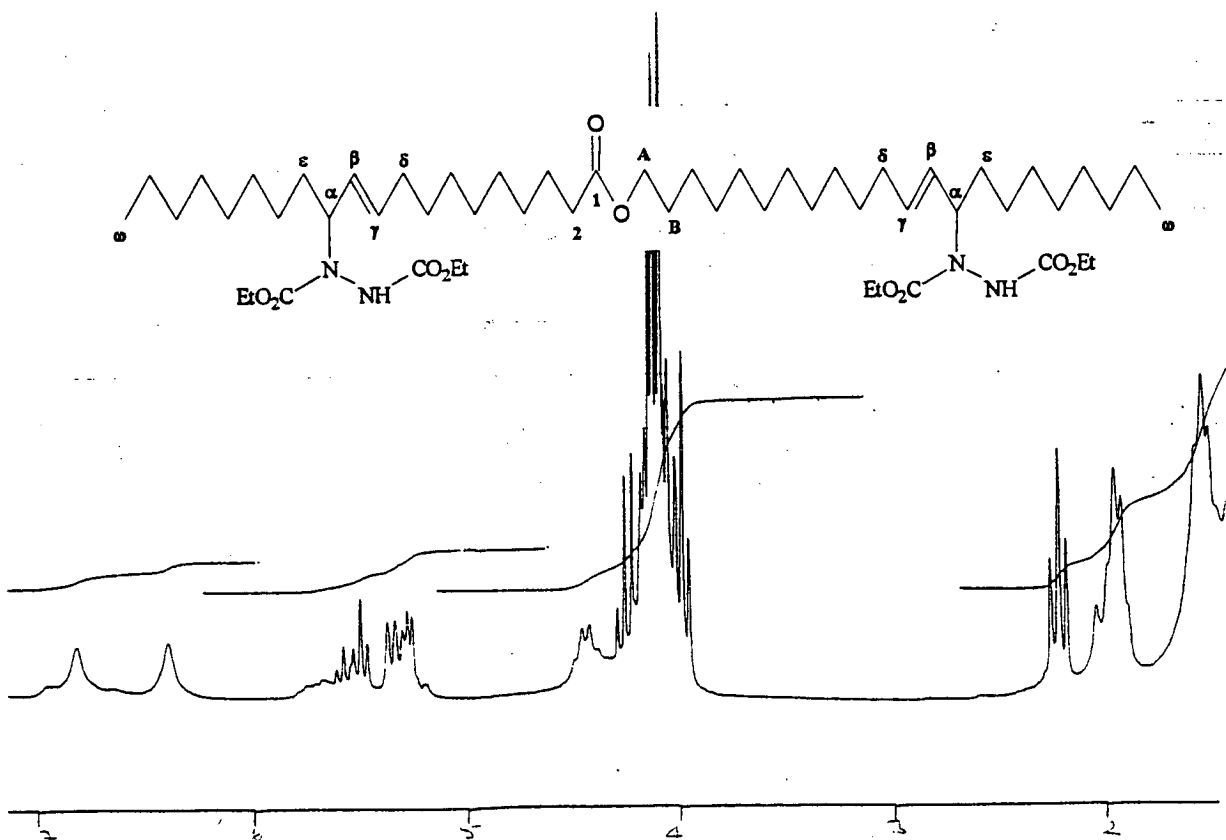


Figure 6



**Spectrum 4: Jojoba & DEAD monoadduct (24)**  
 $^1\text{H}$  NMR (200 MHz)

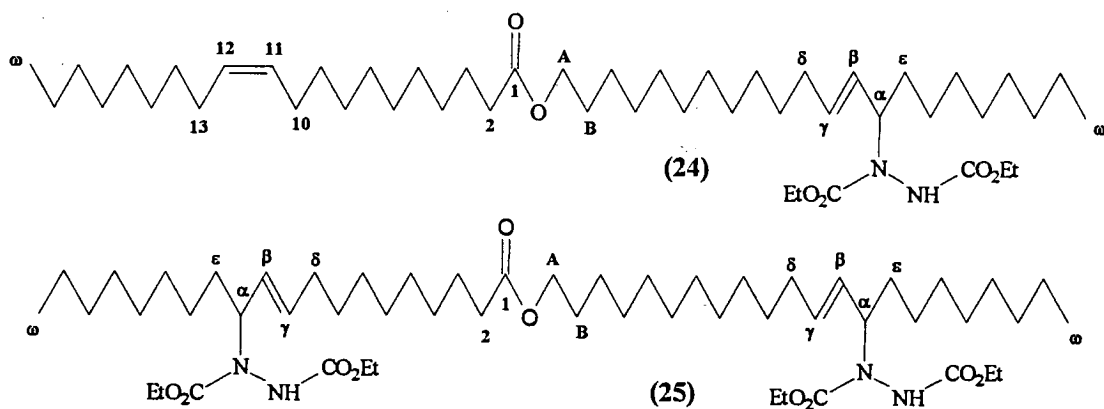


**Spectrum 5: Jojoba & DEAD diadduct (25)**



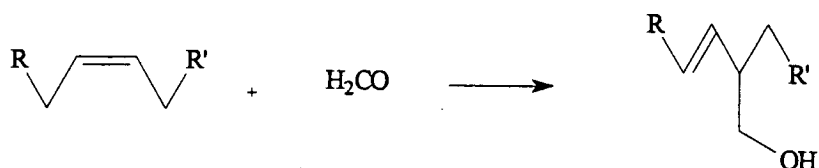
#### 2.2.2.4 Modification of Jojoba

Having completed these model studies with monounsaturated lipid esters, the addition of DEAD to jojoba oil itself was carried out. A 2:1 mixture of DEAD and jojoba oil was heated in 1,1,1-trichloroethane at 75°C for 33 hours to furnish a yellow oil.  $^1\text{H}$  NMR examination of the crude mixture indicated that 68% of the double bonds had undergone reaction. Separation of the products yielded 37 per cent and 35 per cent respectively of the 1:1 and 2:1 adducts (represented by structures 24 & 25), in addition to some unreacted jojoba oil (19%). The proton spectra of these two types of adduct are illustrated in Spectra 4 and 5. It can be seen that the fraction composed of jojoba modified at both double bonds also contained traces of a contaminant ( $\delta_{\text{H}}$  5.7 ppm), possibly caused by further DEAD addition to the new *trans* alkene unit. Although polyadducts have not been isolated, the formation of small amounts of highly modified lipids in the model studies suggests that their presence is likely.



### 2.2.3 Formaldehyde as Enophile

The ene addition of formaldehyde to alkenes is a convenient synthetic route to hydroxymethyl substituted unsaturated compounds. Scheme 48 shows a general representation of this reaction. Being primary alcohols, these products will be capable of further functional group interconversions by reaction with, for example, acyl halides, carboxylic acids and isocyanates, by dehydration or further oxidation. A range of derivatives should therefore be readily accessible.



Scheme 48

The product resulting from ene addition of formaldehyde to vegetable oils (Scheme 48) is an analogue of castor oil. Castor oil's major fatty acid constituent (90%) is ricinoleic acid (12-hydroxyoctadecenoic acid, Figure 7) which, like the ene adduct, contains an alcohol substituent at one of the homoallylic positions. The difference is that the hydroxyl group in castor oil is secondary while the ene adduct bears a primary alcohol.

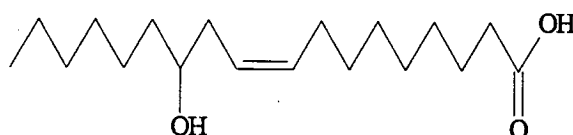


Figure 7

Castor oil has a variety of commercial applications. After dehydration (to form both conjugated and non-conjugated dienes) its major use is as a drying oil in paints and varnishes, while the hydroxyl group in the oil can be esterified with

sulfuric acid to produce an excellent wetting agent.<sup>80</sup> Its derivatives are used in nylon manufacture, in perfumes, polymers and lubricants. During the First World War, aircraft engines were of the rotary type and had to be lubricated *via* the fuel feed. Castor oil was used for this purpose in concentrations of up to 30% and today small quantities of aviation grade lubricant (eg. Castrol R40) are still manufactured for use in these antique aeroplanes.<sup>154</sup> As the lubricant is combusted with the fuel, a characteristic (and evocative) smell is produced.

The ene addition of a formaldehyde to an alkene is closely related to the Prins reaction which involves acid catalysed addition at temperatures of 50 - 115°C. It is reported<sup>154a,b</sup> to give a mixture of products including the predicted ene adduct, as well as several ring structures and a diol (see Scheme 11, Section 1.3.3). In comparison, the Lewis acid catalysed ene addition is highly selective and can be carried out at 0°C.

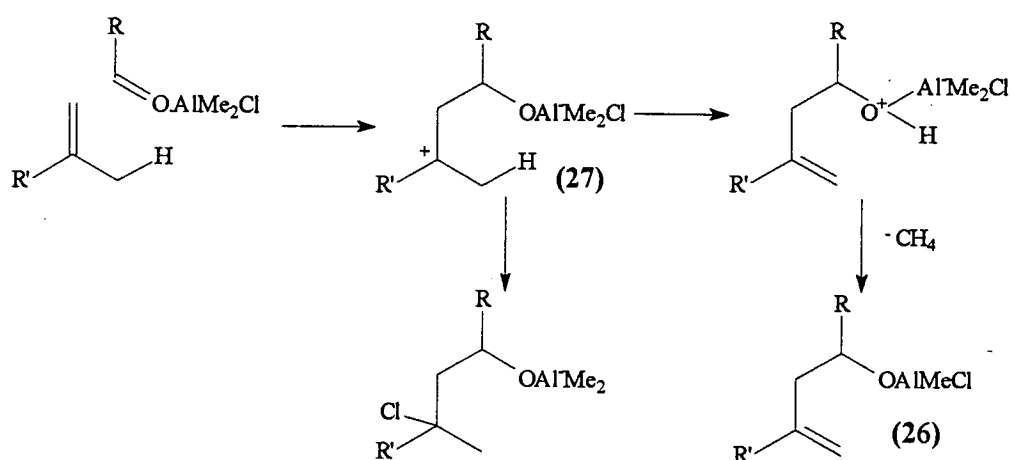
#### 2.2.3.1 Mechanism of Catalysis

The ene addition of carbonyl compounds to alkenes provides a promising synthetic route to homoallylic alcohols. Thermally, the addition of electron deficient aldehydes (such as chloral or methyl glyoxylate) takes place between 100 and 200°C while formaldehyde reacts at 180°C. Vinyl compounds, such as methyl acrylate, methyl methacrylate, methyl vinyl ketone and acrylonitrile react with simple alkenes on heating at 200-300°C for 0.15-9 hours.<sup>155</sup> The use of Lewis acid catalysis allows reaction at 0°C or below by complexation of the Lewis acid which effectively withdraws electrons from the enophile thus (as with a dienophile in the Diels-Alder cycloaddition) accelerating the reaction (see Scheme 7, Section 1.3.1). Snider has carried out extensive studies on the subject covering a variety of enophile types (aldehydes<sup>156</sup> and acrylate esters<sup>157-159</sup>),

using several catalysts, predominantly alkylaluminium halides<sup>160-162</sup> and has also probed the reaction mechanism<sup>163</sup> by using kinetic isotope effect measurements. The results indicated that the reaction is stepwise, proceeding through a complex mechanism involving the formation of either a three membered ring intermediate, a rapidly equilibrating pair of zwitterions or a  $\pi$ -complex between the ene component and the enophile-catalyst, as previously illustrated in Scheme 2, Section 2.

### 2.2.3.2 Choice of Catalyst

Snider also found that the use of alkylaluminium halides, rather than simple metal halides, extends the scope of the reaction as they prevent proton catalysed side reactions which could cause polymerisation of the alkene and isomerisation of double bonds present. Metal halide-enophile complexes are susceptible to solvolysis, yielding a strong acid which can protonate the alkene double bond or ene adduct. The alkylaluminium halide complexes, however, decompose to non-basic aluminium alkoxides which do not undergo these side reactions.<sup>162</sup> For example, in the dimethylaluminium chloride catalysed addition of aldehydes the reaction mechanism can be envisaged as in Scheme 49.



Scheme 49

After 1,5-proton shift the ene adduct-catalyst complex loses methane to form complex (26), which leads to the final alcohol on hydrolytic work-up. By-products of this reaction, when one equivalent of catalyst is used, are chloro-alcohols which are formed when the intermediate carbocation (27) is secondary. When 1.5 to 2 equivalents of catalyst are used, the chloro-alcohols are unstable and are converted to ene adducts.

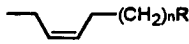
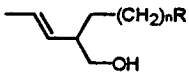
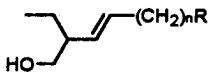
Snider<sup>164</sup> reports the general reactivity order in Lewis acid catalysed ene additions as 1,1-di > tri > tetra >> mono > 1,2-disubstituted alkenes. As the ene components in the present work are predominantly 1,2-disubstituted, care was taken in choosing a suitable catalyst. A further problem with dimethylaluminium chloride is that the methyl group can also act as a nucleophile and can add to the aldehyde.<sup>156</sup> This precludes the use of mono and 1,2-disubstituted alkenes with aldehydes other than formaldehyde. Even with formaldehyde this unwanted addition can occur when non-nucleophilic alkenes are used.

Ethylaluminium dichloride gives better yields in the addition of unreactive alkenes to aldehydes than  $\text{Me}_2\text{AlCl}$  or  $\text{Et}_2\text{AlCl}$  as it is a stronger Lewis acid and its less nucleophilic alkyl groups do not add to the alkene to form by-products.

### 2.2.3.3 Choice of Enophile

Formaldehyde was chosen as the enophile for lipid modifications in the present work as the literature indicated that attempted additions of higher aldehydes (benzaldehyde and acetaldehyde) to 1,2-disubstituted alkenes had been unsuccessful.<sup>156</sup> On the other hand, the addition of formaldehyde to *cis*-alkenol derivatives (28) gave mixtures of products (29 & 30) as shown in Table 6.

Table 6

Reactant  (28)	Total Yield of (29) & (30) (%)		Ratio of (29):(30)
	 (29)	 (30)	
n = 1 R = OH	43		100:0
1 OAc	59		100:0
2 OH	63		80:20
2 OAc	64		82:18
3 OH	50		67:33
3 OAc	81		69:31
3 H	75		44:56

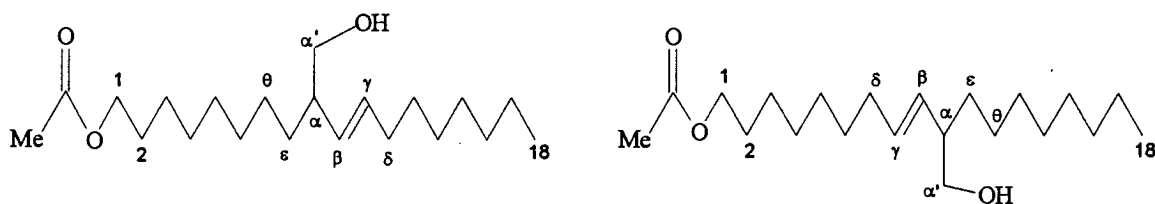
From the data in Table 6, it is evident that the selectivity of 29 over 30 is reduced sharply as the chain length between the double bond and the acetate or alcohol group is increased (*ie.* as the value of *n* increases). The regiochemistry of formaldehyde addition shows that the major product results from formation of the carbocation furthest from the electron withdrawing substituent. Predictably, the inductive effect is reduced with increasing chain length and the product ratios change from 100:0 to *ca.* 70:30 for the acetate substrates.

The present study builds on Snider's work by applying the catalysed ene addition of formaldehyde to jojoba oil. In order to fully understand the reaction, a longer chain acetate and a long chain methyl ester were also modified as models for jojoba oil.

#### 2.2.3.4 Oleyl Acetate as a Model Compound

The presence of the ester functionality in the alkene means that a second equivalent of the Lewis acid is required to allow complexation both to the formaldehyde and to the ester carbonyl within the ene component. The reactions were carried out by adding the Lewis acid (in solution) *via* a syringe to a stirred solution of paraformaldehyde and alkene in dry dichloromethane under nitrogen in a flame-dried flask which was cooled in an ice bath. After one hour the reaction mixture was quenched by dilution with ether followed by slow addition of water until gas evolution ceased. The solution was stirred until the precipitated alumina dissolved and the organic layer was separated, washed, dried and submitted to dry flash column chromatography to furnish the products.

Oleyl acetate reacted to yield 7% of recovered starting lipid and 82% of an oil whose IR spectrum contained a broad absorption centred at  $3448\text{ cm}^{-1}$  (OH). The products were assigned as 31A&B on the basis of their  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra.



(31 A&B)

The alkene protons appeared at 5.09 and 5.45 ppm. The splitting patterns of H- $\beta$  and H- $\gamma$  were more complex than expected and appeared as two doublets of doublets of triplets (2x ddt) and two doublets of triplets of doublets (2x dtd). Two explanations were considered to account for this observation: either a long range coupling between the alkenes and one of the  $\alpha'$  protons, or the presence of the two regioisomers (31 A&B). Decoupling experiments and the use of different

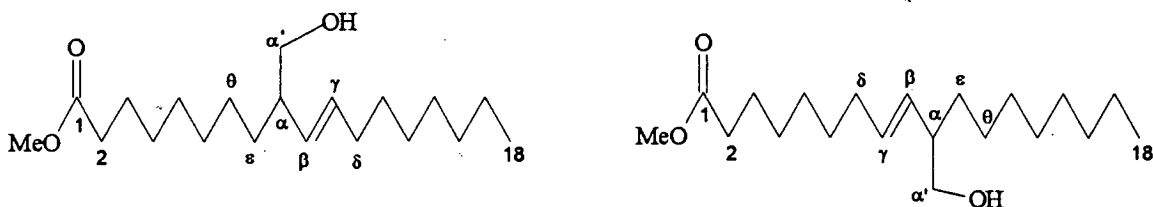
field strengths revealed that the extra peaks were not due to a four-bond coupling but were consistent with the latter option. Once again the large coupling of 15.3 Hz indicated *trans* geometry of the new double bond. The  $\alpha'$  protons are diastereotopic (being adjacent to the chiral centre at  $\alpha$ ) and give rise to a well defined pattern of two doublets of doublets (at 3.28 and 3.44 ppm) with a mutual coupling of 10.4 Hz. This is typical for the geminal protons of a hydroxymethyl group. *J* values of 5.3 and 8.1 Hz were measured for the couplings of  $\alpha'_A(H)$  and  $\alpha'_B(H)$  to  $\alpha(H)$ . The allylic CH( $\alpha$ ) where the enophile becomes attached appears at a lower  $\delta$  value than with any of the previous azo enophiles as it is now adjacent to another carbon atom rather than an electronegative nitrogen.

Under FAB mass spectroscopy conditions the  $M^++1$  peak was small (at  $m/z$  341) while the fragment formed by loss of water at 323 was the major peak. Accurate mass measurements confirmed the identity of the addition products (31A&B) and that of the dehydrated fragment (presumably a conjugated diene). NMR and IR spectra both show OH absorptions and no sign of further unsaturation and it is therefore concluded that the dehydration is only occurring during the FAB mass spectroscopy process.

#### 2.2.3.5 Methyl Oleate as a Model Compound

Methyl oleate, the model for the acid derived portion of jojoba, was reacted as for oleyl acetate and, after solvent removal and chromatography, yielded 33% recovered methyl oleate which was found to be unisomerised by examination of the allylic signals (at *ca.* 27 ppm) by  $^{13}C$  NMR. The major product, isolated in 63% yield, was identified as the ene adducts (32 A&B) by  $^1H$  and  $^{13}C$  NMR (Appendix 12).





(32 A&B)

Once again, in the mass spectrum, the molecular ion peak was weak in comparison to the fragment formed by loss of water.

During the course of this work it was reported that Metzger and Biermann have also carried out ethylaluminium dichloride-catalysed additions of formaldehyde to methyl oleate.<sup>165</sup> Although their reaction procedure differed from ours, in that they used two moles of formaldehyde per mole of lipid but still only use two moles of catalyst, their results are very similar to ours in yield (63%), product geometry (wholly *trans* as determined by GC) and regioselectivity (equimolar amounts of 32 A&B). Their <sup>1</sup>H and <sup>13</sup>C NMR spectra are also consistent and they quote both a molecular ion peak and a fragment due to loss of water in their mass spectral data. They adopted a similar approach, studying vegetable oils as renewable raw material sources and they also studied the alcohols and acids derived from C18:1 lipids with the double bonds at both the 9 and 6 positions. They did not, however, modify the oils themselves, whereas the present work has been extended to cover the addition of formaldehyde to jojoba oil.

### 2.2.3.6 Modification of Jojoba

The addition was carried out as described previously for the model compounds and the products isolated by dry flash chromatography in the yields shown in Table 7.

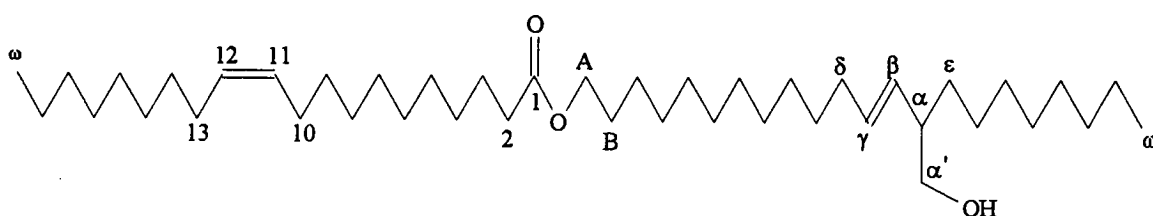
Table 7

Reactant Ratios				Product Yields		
	jojoba	CH <sub>2</sub> O	EtAlCl <sub>2</sub>	recovered jojoba	mono-adducts	di-adducts
i)	2.5 mmol	2.75 mmol	5.5 mmol	54%	30%	8%
ii)	2.5 mmol	5.5 mmol	8.25 mmol	10%	32%	52%
iii)	2.5 mmol	7.5 mmol	10.25 mmol	5%	31%	57%

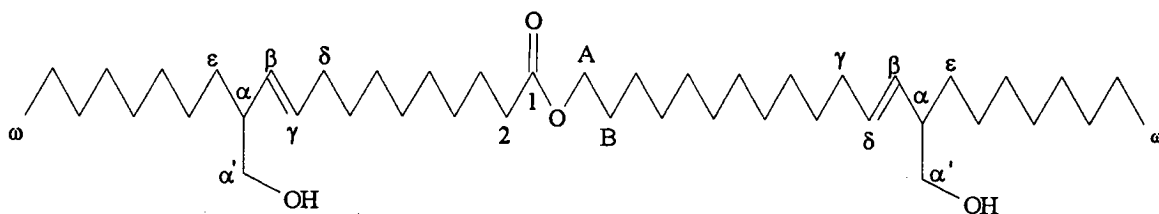
After solvent removal, <sup>1</sup>H NMR spectra of the first two crude reaction mixtures were obtained and comparisons made of the integrals of the methylene peak adjacent to the ester in jojoba (CH<sub>2</sub>OCO) *versus* the methylene signal of the hydroxymethylene substituent. These signals are well resolved from the rest of the spectrum and appear at *ca.* 4.0 and 3.3 - 3.5 ppm respectively. By this method the levels of modification were estimated as 21% and 70%. These values are consistent with the quantities of each adduct type which were later isolated by dry flash chromatography (as displayed in Table 7). The percentages of double bonds modified (measured for the isolated adducts) were 23% and 68% for the first two reactant ratios.

Analysis by <sup>1</sup>H and <sup>13</sup>C NMR of the purified products revealed that the first fraction (after removal of unreacted jojoba oil) consisted of the oil modified at one of its two double bonds, with the other double bond still remaining with *cis*

geometry. Evidence for this is seen in the residual allylic signal which occur at *ca.* 27 ppm (rather than at 32 ppm which would be the case for *trans* geometry). The fraction will comprise a mixture of similar components, both as a result of the composition of the oil itself and because the enophile can become attached at four distinct positions in each molecule. Compound 33 is an example of this type of adduct.

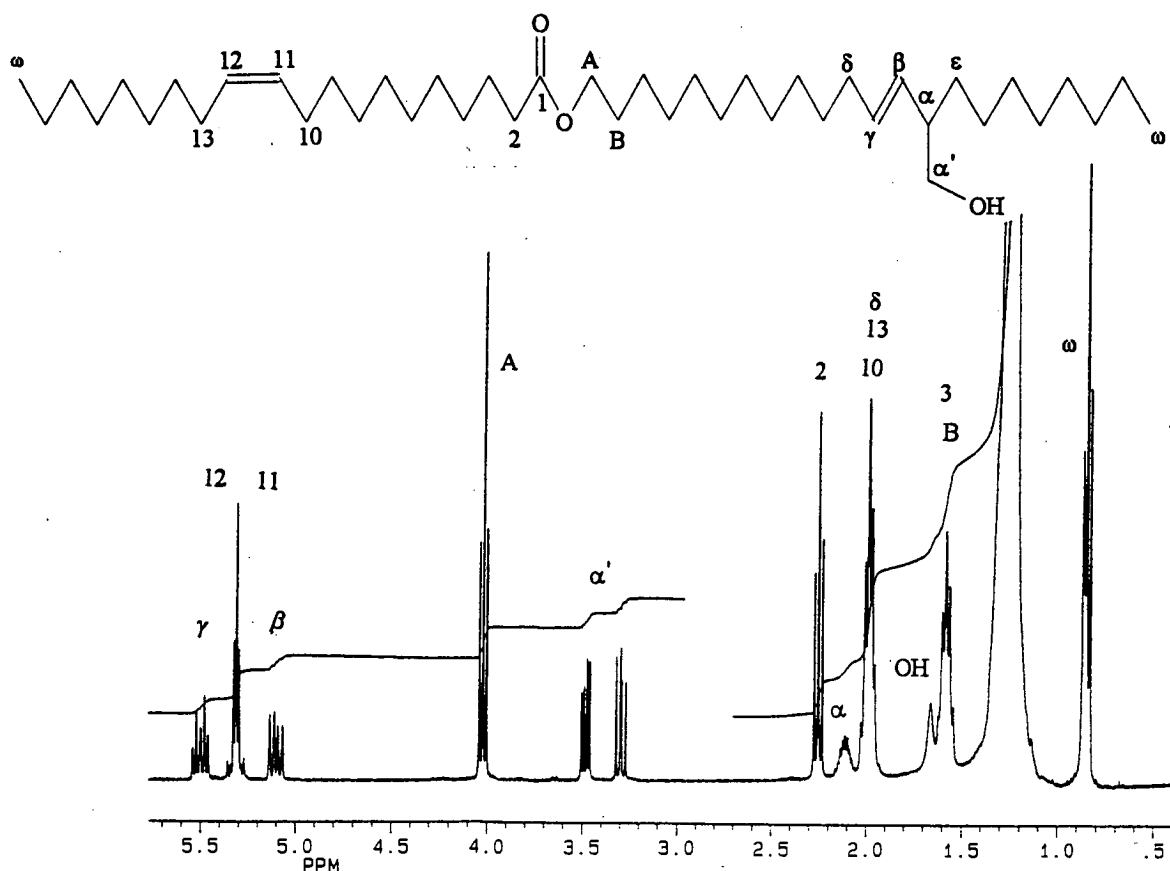


(33)

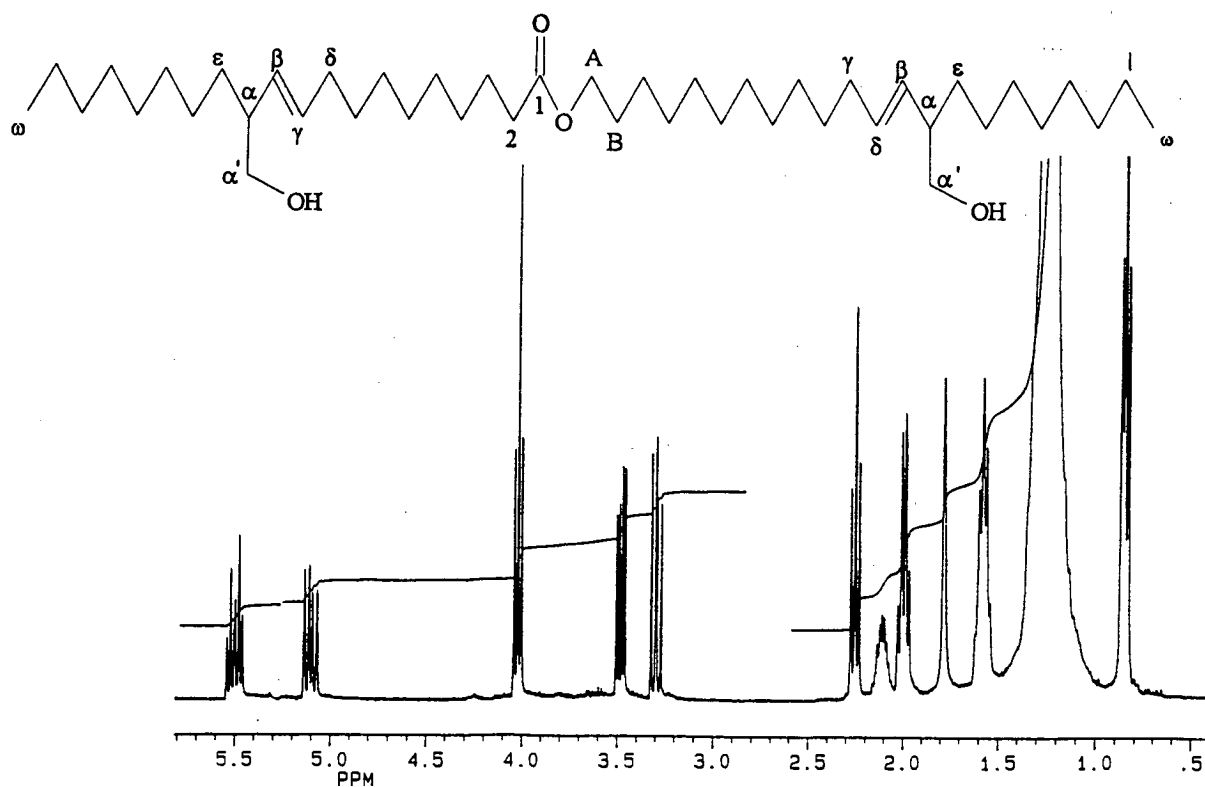


(34)

The more polar fraction from the column consisted of the oil modified at both double bonds. Compound 34 shows an example of such a dihydroxymethyl-jojoba (DHMJ) adduct. Spectra 6 and 7 show the  $^1\text{H}$  NMR spectra of the mono- and di-adducts of formaldehyde with jojoba. For full NMR spectral assignments see Appendices 14 and 15. Once again under FAB mass spectroscopy conditions the adducts readily dehydrated to form dienes.



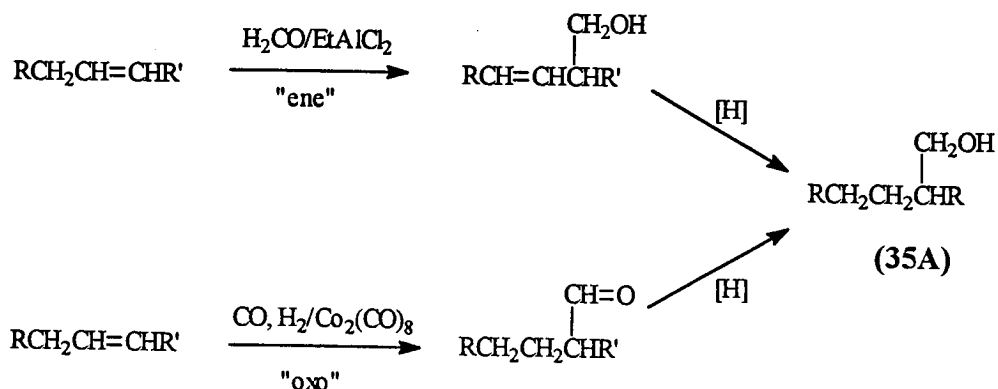
**Spectrum 6: Jojoba & Formaldehyde monoadduct (33)**  
 $^1\text{H}$  NMR (360 MHz)



**Spectrum 7: Jojoba & Formaldehyde diadduct (34)**

### 2.2.3.7 Hydrogenation of Dihydroxymethyl-Jojoba (DHMJ) (34)

Further modifications on the new difunctional jojoba oil adduct (DHMJ) were carried out. Firstly, the adduct was hydrogenated to give the saturated analogue of the dialcohol (35A). The product is similar to that which would be obtained *via* the Oxo process,<sup>154b</sup> involving the catalysed addition of carbon monoxide and hydrogen to an alkene; in this case jojoba oil (Scheme 50).



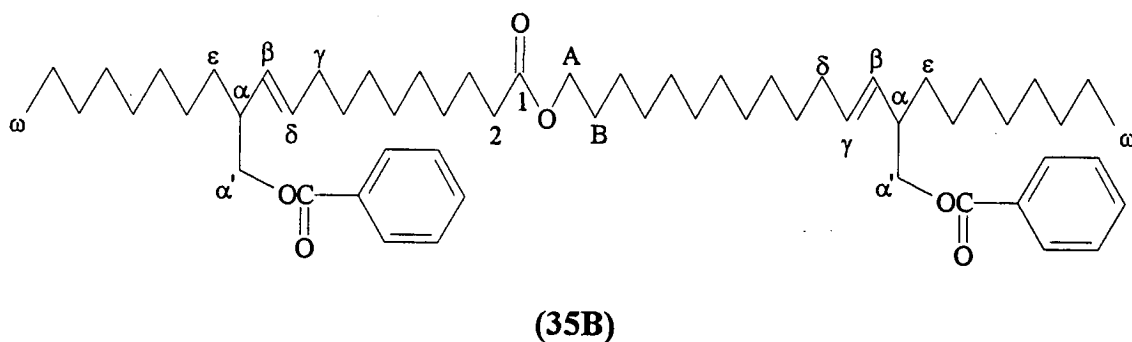
Scheme 50

The hydrogenation was carried out using palladium on activated charcoal as a catalyst under an atmosphere of hydrogen. The product (35A) was a colourless oil and was isolated in 70% yield. Comparison of its  $^1H$  NMR spectrum with that of DHMJ revealed that the signals from the alkene at 5.0 - 5.6 ppm in the  $^1H$  and 131 and 134 ppm in the  $^{13}C$  NMR spectra had been completely removed while the  $\alpha'$  methylene absorptions had collapsed from their complex diastereotopic pattern of two doublets of doublets to a doublet at 3.51 ppm ( $J$  5.2 Hz). This is expected as C- $\alpha$  is no longer effective as a chiral centre (because the removal of the adjacent double bond effectively makes the two long alkyl chains indistinguishable). Under FAB ms conditions, the molecular ion peak was detected ( $M^++1 = 681$ ) as well as peaks corresponding to loss of one and two molecules of water (at 661 and 645). Although the unsaturation had been

removed so that loss of water could no longer form a conjugated diene, the saturated product still underwent the same fragmentation to give peaks in the mass spectrum due to loss of water.

#### 2.2.3.8 Benzoylation of Dihydroxymethyl-Jojoba (DHMJ) (34)

The hydroxymethyl groups in DHMJ were converted to the benzoate ester derivative by treatment with two equivalents of benzoyl chloride. The reaction was maintained at 100°C with a stream of nitrogen bubbling through it to remove HCl gas and was high yielding (94%). The product was identified as (35B) from its NMR spectra.



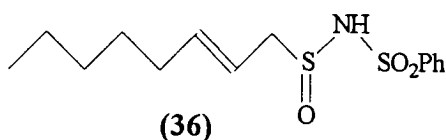
The characteristic features in the  $^1\text{H}$  NMR spectrum show that the  $\alpha$ -CH signals have shifted to a higher  $\delta$  value from 2.11 to 2.44 ppm, while the OH absorption has disappeared. The alkene protons  $\beta$  and  $\gamma$  have retained their characteristic splittings of a doublet of doublets and a doublet of triplets with a mutual coupling of 15.3 Hz and although the two  $\alpha'$  protons are still adjacent to a chiral centre ( $\alpha$ ), they no longer display their characteristic pattern of two doublets of doublets but collapse to a doublet at 4.19 ppm.

Under FAB ms conditions this adduct underwent a facile fragmentation by loss of two molecules of benzoic acid which resulted in the fragment with  $m/z$  ( $M^{++1}$ ) = 643 being the major signal rather than the molecular ion peak at ( $M^{++1}$ ) of 887.

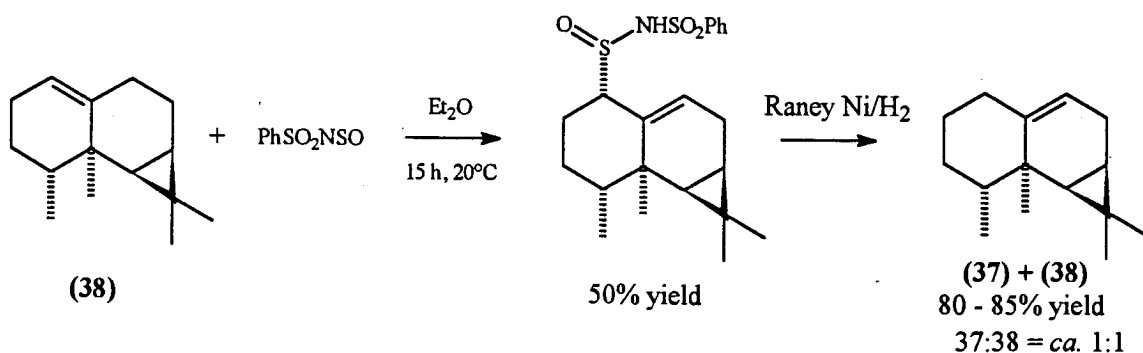
In conclusion, it has been shown that hydroxymethyl substituents can readily be added to jojoba oil and furthermore that these adducts can be modified in high yielding reactions to form a variety of new compounds. A possible extension to this work would be to investigate the reaction of difunctional acyl halides *eg.* the 1,2-, 1,3- and 1,4-disubstituted phenyl analogues (phthaloyl, isophthaloyl and terephthaloyl dichloride) with DHMJ. These combinations should result in the formation of polymers and the use of different difunctional acyl chlorides could result in changing polymeric properties. The corresponding reactions with diisocyanates would afford polyurethanes and this reaction path could also be investigated.

#### 2.2.4 *N*-Sulfinyl-*p*-toluenesulfonamide (TosNSO) as Enophile

Kresze describes compounds containing a sulfur nitrogen double bond as "super-enophiles"<sup>166</sup> as they have the ability to convert alkenes rapidly to the expected ene addition products at ambient temperatures or below. He has systematically investigated the synthesis, cycloadditions and other reactions of *N*-sulfinyl compounds ( $\text{RN}=\text{S}=\text{O}$ )<sup>167</sup> and has studied the effects of varying alkyl substituents on their enophilic activities.<sup>168</sup> His work also extends to the study of sulfur diimide compounds ( $\text{RN}=\text{S}=\text{NR}'$ ).<sup>169,170</sup> The benzenesulfonyl analogue ( $\text{PhSO}_2\text{NSO}$ ) addition to some terminal and cyclic alkenes has been reported to give between 33 and 85% yield of ene adducts with reaction times varying between 2 and 48 h.<sup>171</sup> For example, the reaction of 1-octene in benzene furnished adduct (36) in 75% yield after 48 h.



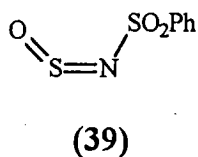
The same enophile has been utilised to effect an isomerisation reaction; ene addition of *N*-sulfinylbenzenesulfonamide to calarene (38) followed by desulfurisation afforded aristolene (37) (Scheme 51).<sup>172</sup>



Scheme 51

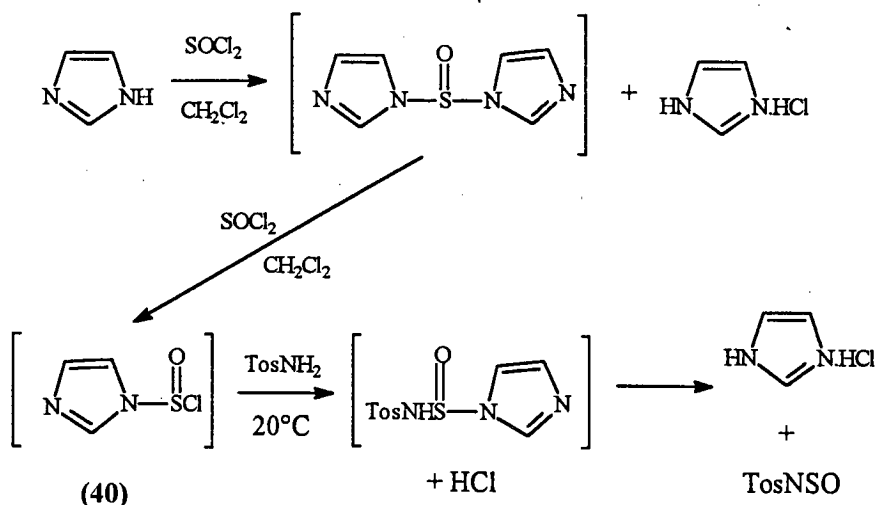


The high reactivity of this system may be associated with *cis* geometry of the enophile. X-ray structure analysis of *N*-sulfinylbenzenesulfonamide (PhSO<sub>2</sub>NSO) (39)<sup>173</sup> shows that the compound has *cis* configuration. Possession of such a *cis* geometry is known to increase enophilic activity. For example, PTAD is an excellent enophile and the reactivity of DEAD is increased on irradiation to form the *cis* isomer from the *trans*.



In view of its reported high reactivity, coupled with the ability to introduce both nitrogen and sulfur heteroatoms (which are generally desirable components in friction reduction additives) it was decided to investigate the use of the tosyl-substituted *N*-sulfinyl enophile to modify jojoba oil.

There are several methods in the literature for the preparation of arenesulfinylsulfonamides, including the reaction of an excess of thionyl chloride with the sulfonamide in refluxing benzene;<sup>167</sup> more recently, the addition of 1% *N,N*-dichloro-*p*-toluenesulfonamide has been reported to decrease the reaction time.<sup>174</sup> An alternative approach<sup>175</sup> is sketched in Scheme 52 where the sulfonamide is treated with *N*-(chlorosulfinyl)imidazole (40) *in situ* to furnish the desired enophile in almost quantitative yield at 20°C under mild conditions.



**Scheme 52**

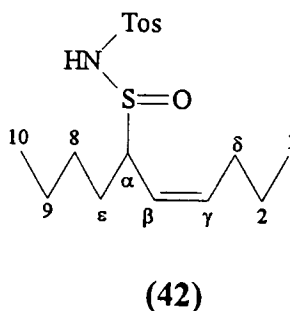
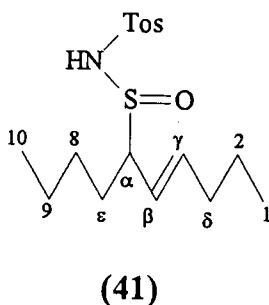
A modified version of the first approach was adopted, however problems were initially encountered in the synthesis of *N*-sulfinyl-*p*-toluenesulfonamide (TosNSO) from *p*-toluenesulfonamide using toluene as the solvent. On Kugelrohr distillation, *p*-toluenesulfonyl chloride was isolated as a major product; identified by FTIR and its melting point (66°C). In a repeat experiment the solvent was omitted and the amide refluxed in thionyl chloride at 80-90°C for 8.5 h. After removal of excess thionyl chloride, the resulting orange oil was submitted to Kugelrohr distillation (125°C, 0.02 mbar) to yield a yellow oil which solidified on cooling (26%). The IR spectrum (nujol mull) contained absorptions at 1300 and 1160 cm<sup>-1</sup> (N=S=O)<sup>176</sup> and at 1380 (SO<sub>2</sub>). Contamination by a small amount of *p*-toluenesulfonamide was indicated by a pair of absorptions at 3350 and 3260 cm<sup>-1</sup> (NH symmetrical and unsymmetrical stretches). From integration of the methyl signals in the <sup>1</sup>H NMR spectrum it was estimated that the product contained *ca.* 9% of *p*-toluenesulfonamide. The source of this impurity could be from residual starting material or, as the enophile is extremely hygroscopic,<sup>175</sup> it could be formed *via* hydrolysis of the product by atmospheric moisture. Attempts

at further purification were unsuccessful and so the enophile was used as described.

An alternative synthesis was attempted by Veit Bolik (an *Erasmus* exchange student from Kaiserslautern, Germany). He followed the chlorosulfinylimidazole procedure (Scheme 52) and reported a crude yield of 78% TosNSO. However, on purification by Kugelrohr distillation, the enophile decomposed and so this synthesis was not pursued.

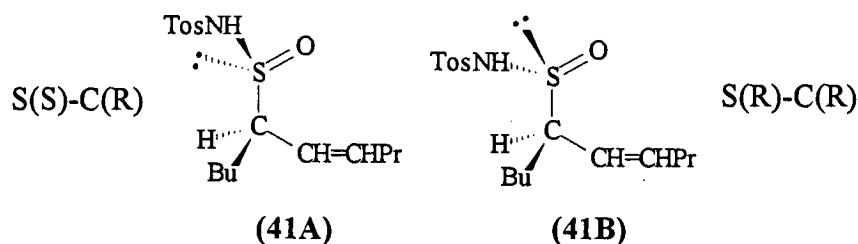
#### 2.2.4.1 *Cis*-5-Decene as a Model Compound

A 2:1 mixture of *cis*-5-decene and the sulfinyl enophile was reacted in dry dichloromethane. The initial addition was carried out at -30°C and the mixture allowed to warm to room temperature before stirring for 24 hours. The colour faded from yellow to colourless and after solvent removal the crude yield was 87%. Dry flash column chromatography was carried out in order to isolate the ene adduct. *p*-Toluenesulfonamide was identified (as a by-product) from its <sup>13</sup>C NMR and melting point (42% w.r.t. TosNSO). This was already present as a contaminant in the enophile at a level of *ca.* 9% and could also have been formed during the reaction. Elution with 100% ethanol was required to remove the most polar fraction which contained the ene adduct in 41% yield (w.r.t. TosNSO). Examination of this fraction by <sup>13</sup>C NMR revealed some unexpected doubling of peaks. The structure of the adduct (41) was assigned on the basis of its spectroscopic properties.



The signal at C- $\alpha$  was clearly doubled (67.33 & 67.93 ppm), as were those for C- $\beta$  and C- $\gamma$  (122.57 & 123.96 ppm and 137.87 & 137.87 ppm respectively). The  $^1\text{H}$  NMR spectrum also revealed more complex alkene signals than those found for the previous azo adducts. For example, H- $\beta$  appeared as two sets of doublets of doublets of triplets. In both cases the large splitting was *ca.* 15 Hz, consistent with *trans* alkene geometry. The extra set of signals cannot therefore be due to the formation of the *cis* isomer (42). The ratio of the two sets of signals was estimated as 62:38 from the integrals at H- $\beta$ . The presence of two components was also visible in the signals from H- $\alpha$  and H- $\gamma$ .

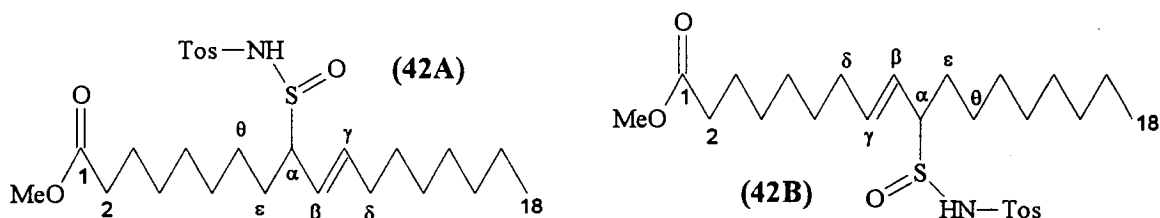
The most likely explanation of this phenomenon is the presence of the tricoordinated sulfur atom adjacent to C- $\alpha$ . As both these centres are chiral, two diastereomeric pairs (41A & 41B) can be formed in this addition.



The asymmetric nature of the sulfur atom in TosNSO/ene adducts has been demonstrated by Bussas *et al*<sup>177</sup> who have reacted a chiral ene component, (S)-(+)-3-phenyl-1-butene, with TosNSO and measured the enantiomeric excess of the adduct (40 +/- 5%) as well as the absolute configuration of the predominant enantiomer (R). They also noted, as in the present case, that none of the *cis*-isomer was detected in the NMR spectra of the product.

#### 2.2.4.2 Methyl Oleate as a Model Compound

Equimolar quantities of methyl oleate and TosNSO were stirred at 0°C in dry dichloromethane for 24 h. After removal of the solvent, the residue was submitted to dry flash column chromatography yielding, in order of elution: methyl oleate (26%), TosNSO (42%) and the ene adduct, (42A&B) (45%). The product was identified from its NMR data by comparison with the model decene adduct. Once again the carbon signals in the NMR spectrum corresponding to positions  $\alpha$ ,  $\beta$ ,  $\gamma$ , and  $\delta$  showed doubling. The extra signals which had been noted in the *cis*-5-decene model adduct spectrum (caused by the two sets of diastereomers) were also observed in the  $^1\text{H}$  NMR spectrum of the methyl oleate adduct as broadened signals, especially that of H- $\beta$ . Unfortunately the signals were not well enough resolved to make an estimate of the relative proportions of the diastereomers.



On examination of the recovered methyl oleate by  $^{13}\text{C}$  NMR it was noted that it had isomerised to 80% of its *trans* isomer, methyl elaidate. In previous ene additions, the recovered alkenes had been examined for any structural changes and none had been observed. This is the first example, in this work, of an isomerisation taking place. In the literature, no specific discussion of the ene component geometry have been found except where Hori *et al*<sup>175</sup> used the retro-ene reaction to introduce deuterium or tritium into the allylic position of alkenes. They induced the retro reaction by refluxing ene adducts in benzene for 7.5 - 14 h but also commented that the reaction occurred over a few days of the adduct

standing in moist air. The retro-ene reactions of *cis* and *trans*-5-decene/TosNSO adducts both resulted in isolation of the same mixture of 23% *cis* and 77% *trans*-5-decene. It is likely that, in this work, during isolation of the reaction products, this retro-ene isomerisation occurred to form methyl elaidate.

#### 2.2.4.3 Modification of Jojoba Oil

Jojoba (1 equivalent) was stirred with 2 equivalents of TosNSO (to allow for the two double bonds per molecule) in dry dichloromethane for 24 h. After dry flash chromatography 40% of jojoba was recovered and  $^{13}\text{C}$  NMR spectroscopy revealed that the double bonds remained *cis*. This is in contrast to the methyl oleate model study where 80% isomerisation occurred. No definite explanation can be offered for this divergent behaviour although a possibility is that for the methyl oleate reaction the mixture was kept for a period before purification and, during that time, it may have undergone a partial retro-ene reaction as described by Hori *et al.*,<sup>174</sup> whereas the jojoba adducts were isolated more quickly.

Toluenesulfonamide was again isolated as a byproduct of the reaction in 38% yield by eluting with 100% ether. Two types of adduct were expected, corresponding to jojoba modified at one double bond and at both double bonds. Both these adducts proved to be highly polar and were eluted from the column together (53% yield). Attempts to separate the 1:1 from the 2:1 adducts by preparative TLC were only partially successful and resulted in the loss of some of the sample. The  $^{13}\text{C}$  NMR spectrum of the purified 1:1 adduct (42C) was obtained and showed residual unmodified double bond signals at 27.01 and 129.69 ppm (the alkene and allylic positions, indicating *cis* geometry) as well as new signals characteristic of the  $\alpha$ -carbon at 67.99 ppm and the new alkene unit (C- $\beta/\gamma$ ) at 122.53 and 138.19 ppm. Once again there was evidence in the  $^1\text{H}$

NMR spectrum of two sets of diastereomers while the  $^{13}\text{C}$  NMR spectrum clearly showed doubling of both the C- $\alpha$  and alkene signals.

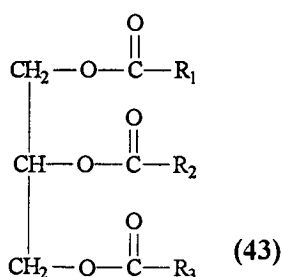
In conclusion, the ene addition of TosNSO to jojoba oil was achieved, in moderate yield, to form a mixture of diastereomers as well as the regioisomers seen for other enophiles. However, the resultant adducts are inherently unstable under moist atmospheric conditions and the reaction also generates a significant quantity of  $\text{TosNH}_2$  as a byproduct.

### 3. VEGETABLE OILS

#### 3.1 Introduction to Vegetable Oils

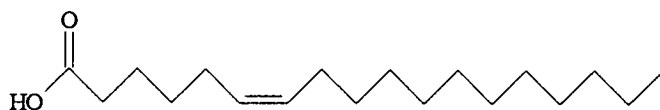
##### 3.1.1 Structure and Nomenclature

This chapter is concerned with the more common types of vegetable oils found in nature; those having a triglyceride structure (43). These tri-esters are derived from glycerol with a variety of carboxylic acids (referred to as fatty acids) which can be saturated, mono- or polyunsaturated.



R = saturated or unsaturated  
hydrocarbon chains,  
generally containing  
7 to 21 carbon atoms.

Their occurrence varies widely among different oil species, however, each oil has its own characteristic composition which does not vary much from sample to sample. The fatty acid compositions of soya bean, palm, sunflower, peanut, cottonseed, and coconut oils (which account for approximately 80% of world production of vegetable oils)<sup>178</sup> are shown in Table 8. In this table, both the non-systematic names and numerical notations are given (eg. 18:2, where 18 is the number of carbon atoms in the chain and 2 is the number of double bonds present). Sometimes the position of the double bonds is indicated by the symbol  $\Delta$  and a number which indicates the double bond position relative to the carboxylate group or by (n-x) where x is the number of carbon atoms from the methyl terminal. For example one of the isomers of oleic acid, petroselinic acid (44), whose systematic name is Z-6-octadecenoic acid, can be designated C18:1  $\Delta$ 6 or C18:1 (n-12).



(44)



Table 8

Non-systematic name and numerical representation	Typical % fatty acid composition for each oil type					
	soya	sun-flower	peanut	cotton-seed	palm	coconut
caproic 6:0						0.5
caprylic 8:0						8.0
capric 10:0						6.0
lauric 12:0				0.1	0.1	47.0
myristic 14:0	0.1	0.1	0.1	1.0	1.0	17.5
palmitic 16:0	11.0	6.5	10.0	22.0	45.0	9.0
palmitoleic 16:1	0.5	0.3		1.0	0.2	
margaric 17:0	0.1	0.1	0.1	0.1	0.1	
margaroleic 17:1			0.1	0.1		
stearic 18:0	3.5	4.0	3.0	3.0	4.5	3.0
oleic 18:1	22.0	21.5	42.0	19.0	38.0	7.0
linoleic 18:2	54.0	66.0	38.0	53.0	10.0	1.8
linolenic 18:3	8.0	0.5		0.3	0.5	0.1
arachidic 20:0	0.5	0.4	1.5	0.3	0.5	0.1
gadoleic 20:1		0.1	1.0			
behenic 22:0	0.3	0.5	3.0	0.1	0.1	

Bold figures are used for compositions  $\geq 1.0\%$

Naturally occurring fatty acids in vegetable oils are virtually always composed of an even number of carbons in the chain and contain *cis* unsaturation rather than *trans*. This reduces the ability of the triglycerides to pack together evenly and results in a lower melting point than for *trans* geometry.

The component fatty acids in triglycerides can also display positional isomerism in that they can become attached to the 1 or 3 external positions in glycerol or to the central 2 position. In summary, there is a wide range of vegetable oils available; each of which is composed of a complex (but characteristic) triglyceride mixture. Compositional analysis of vegetable oils is described in Section 3.1.3.

### 3.1.2 Chemistry and Uses of Vegetable Oils

Industrial oleochemical reactions have predominantly been those occurring at the fatty acid carboxy groups rather than those involving the hydrocarbon chains. Hydrolysis with steam or transesterification with methanol transforms the oils into fatty acids or their methyl esters respectively, plus glycerol. These are the compounds on which oleochemistry are based.

Methyl esters are used in cosmetics while the fatty acids, alcohols, amines and their derivatives find wide application in the chemical industry,<sup>179</sup> as illustrated in Table 9.

Table 9

Fatty acids and derivatives	plastics, metal soaps, washing and cleaning agents, soaps, cosmetics, alkyd resins, dyestuffs, textile, leather and paper industries, rubber, lubricants.
Fatty alcohols and derivatives	washing and cleaning agents, soaps, cosmetics, textile, leather and paper industries, mineral oil additives.
Fatty amines and derivatives	fabric conditioners, mining, road making, biocides, textile and fibre industries, mineral oil additives.

Fatty alcohols are formed from the methyl esters by high pressure hydrogenation at elevated temperatures (200 - 250°C) using mixed metal oxide catalysts. The choice of catalyst controls whether unsaturation in the hydrocarbon chain is retained or removed; for example, copper catalysts give saturated products while a combination of zinc oxide and chromium oxide can be used to preserve any double bonds present.

There are several routes to the production of fatty amines. From the acid, reaction of ammonia gives amides and nitriles as intermediates.

Two major benefits in the use of natural oils and fats as raw materials in the chemical industry is that they are renewable and, in comparison to mineral oil sources, biodegradable. There has been a great deal of interest recently in the use of vegetable oil esters as replacement for diesel fuels.<sup>180</sup> In the UK, a long-term trial on a car fleet is being carried out using rape methyl esters as the fuel in three cars.<sup>181</sup> Although the cost of biodiesel is about twice that of conventional diesel (before tax), subsidies covering industrial crops on set-aside land and the possibility of favourable tax benefits for environmentally



friendly energy sources could reduce the price gap. The glycerol fragment resulting from ester hydrolysis also finds use in cosmetics, toothpaste, pharmaceuticals, foodstuffs, lacquers, plastics, synthetic resins, tobacco, explosives and cellulose processing.

Many of the reactions which have been carried out on the fatty chains in vegetable oils are similar to those described in section 2.1.3 on the chemistry of jojoba, including hydrogenation, epoxidation, metathesis, oxidative scission and addition of halogens. The presence of polyunsaturated fatty acid components, such as linoleic acid (C18:2), give scope for further reactions. It has been reported<sup>179</sup> that when the double bonds isomerise into *trans* conjugation then Diels-Alder cycloadditions with suitable dienophiles are possible.

Alterations to the triglyceride structure can be achieved both chemically and enzymatically by interesterification. The latter method can be highly regiospecific in order to synthesise fats with specified melting behaviours. Fractionation is a physical method which is used to separate an oil into fractions with different melting ranges for different applications, while winterisation is a more simplified type of fractionating process which is used to remove "waxy" components from oils by chilling the oil to *ca.* 0°C, allowing crystals to form and then removing them by filtration.

The majority of intact triglycerides are used in foodstuffs. However, their use in lubricants as additives has recently been reported.<sup>182</sup> The authors describe several formulations based on rapeseed oil and claim benefits as viscosity improvers, friction modifiers, anti-oxidants and extreme pressure and anti-wear additives. The use of castor oil as a lubricant has previously been mentioned in Section 2.2.3. Although vegetable oils have benefits over

mineral oils in that they are readily biodegradable and so seen as environmentally friendly, by the same token they also suffer from being hydrolytically and sometimes oxidatively unstable. In addition, they have a higher viscosity index (VI) and a higher pour point than conventional fluids. The higher VI values can be beneficial as they mean that vegetable oils display less change in viscosity with temperature, while the higher pour point values necessitate the use of pour-point depressant additives. Vegetable oils, unfortunately, do not respond as well as mineral oils to the use of these additives.<sup>183</sup>

In the current climate of environmental awareness, the use of recycled vegetable oils (from sources such as waste frying oil from fast food outlets) has also been reported. For example, the synthesis of a polyurethane foam from used oil with high acid values has been carried out by reaction of the oil with polypropylene glycol and a diisocyanate.<sup>184</sup>

### **3.1.3 Compositional Analysis of Vegetable Oils**

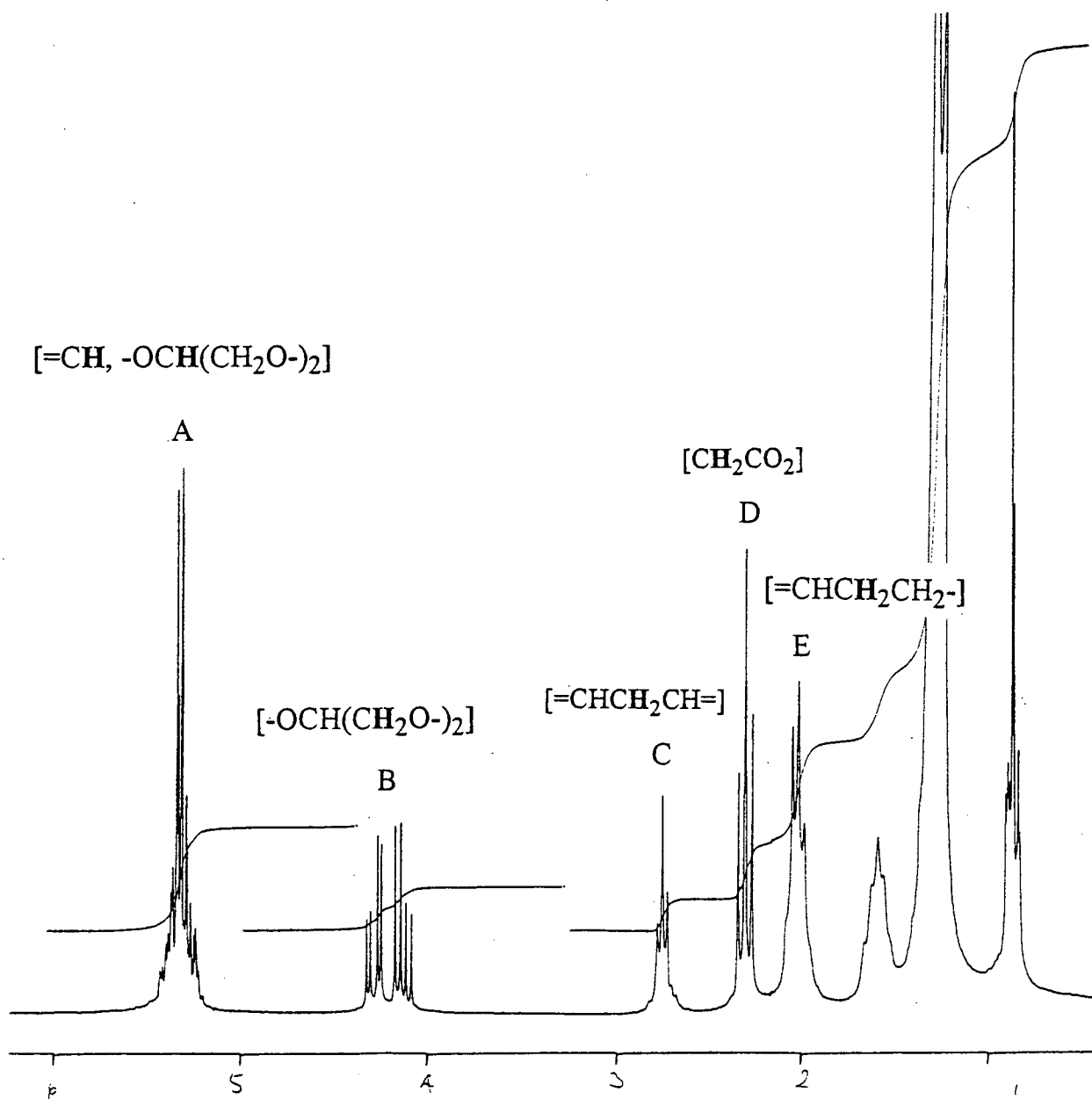
For the purpose of this work, two complimentary analysis techniques were utilised; one chromatographic and the other spectroscopic.

#### **3.1.3.1 Chromatographic Analysis**

Fatty acid methyl ester (FAME) analysis is a standard procedure which is used to identify the proportions of each fatty acid present within an oil sample. The theory and practice of this technique has recently been described.<sup>185</sup> This involves transesterification of the triglycerides into their methyl esters, separation on a capillary GC column and quantification. This procedure was carried out at Castrol (on the oils shown in Table 10) to give detailed information on both chain lengths and unsaturation in the component fatty acids.

% Fatty Acid Composition of Vegetable Oils by FAME Analysis											
	Castor	Grape-seed	Ground-nut	Meadow-foam	Olive	Palm (super olein)	Rape	Safflower	Sesame	Soya	Sunflower (hioleic)
14:0	1.0										
16:0	1.3	6.2	8.9	0.5	9.7	36.8	3.6	6.5	8.1	9.7	6.7
16:1				0.1		0.2					
18:0	2.2	3.5	2.2	0.2	3.3	3.8	1.4	2.6	5.7	4.0	4.9
18:1	4.2	15.7	41.4	2.3	77.7	44.4	51.2	12.3	38.9	23.1	22.9
18:1 Δ11						0.8	3.6				
18:1 (OH)	87.2										
18:2	5.0	73.8	38.5	2.9	8.8	12.5	22.8	78.1	46.2	53.3	62.9
18:3		0.6	2.0			0.2	9.3	0.1	0.4	6.8	0.1
20:0		0.2	1.1	0.7		0.3	1.0	0.4	0.7	0.4	0.4
20:1				60.6			2.0				0.2
20:2				0.1							
22:0			3.4	0.1			1.0			0.3	0.8
22:1			0.2	12.9			1.7				
22:2				18.5							
24:0			2.0								0.3
24:2				0.7							

Table 10



**Spectrum 8: Sunflower Oil  $^1\text{H}$  NMR (200 MHz)**

### 3.1.3.2 Spectroscopic Analysis

The oils were analysed by both  $^1\text{H}$  and  $^{13}\text{C}$  NMR in Edinburgh with the aim of quantifying the relative amounts of saturated, monounsaturated and polyunsaturated fatty acids, without having to derivatise the oil. The resultant spectra were also used for comparison with those of modified oil samples after enophile additions.

#### (i) $^1\text{H}$ NMR Analysis

Spectrum 8 shows the region  $\delta$  2 - 5.5 ppm in the  $^1\text{H}$  NMR spectrum of sunflower oil containing five sets of peaks which are labelled A - E. These peaks result from the following protons:

A = alkene signals plus CH from glycerol fragment	$[=\text{CH}, -\text{OCH}(\text{CH}_2\text{O}-)_2]$
B = glycerol $\text{CH}_2$ signals	$[-\text{OCH}(\text{CH}_2\text{O}-)_2]$
C = doubly allylic signals; found in polyunsaturates	$[=\text{CHCH}_2\text{CH}=]$
D = signals from methylenes adjacent to ester group	$[\text{CH}_2\text{CO}_2]$
E = allylic $\text{CH}_2$ signals	$[=\text{CHCH}_2\text{CH}_2-]$

The size of the integral for each peak (A - E) can be expressed as the sum of the contributions from each type of fatty acid. The following equations can be derived (where S = saturated; M = monounsaturated; D = doubly-unsaturated and T = triply-unsaturated):

Eqn 1	A - B/4	=	6M + 12D + 18T
Eqn 2	B	=	4S + 4M + 4D + 4T
Eqn 3	C	=	6D + 12T
Eqn 4	D	=	6S + 6M + 6D + 6T
Eqn 5	E	=	12M + 12D + 12T

Equations 2 and 4 give the same information and, as the integral measurement for peak B is better resolved, equation 4 is not required. Manipulating the four remaining equations to solve for S, M, D and T gives:



$$\begin{array}{llll}
 \text{Eqn 6} & 1/12 \times (2A - B/2 - E) & = & D + 2T \\
 \text{Eqn 7} & 1/6 \times (A - B/4 - 2C) & = & M + T \\
 \text{Eqn 8} & 1/4 \times (B - E/3) & = & S
 \end{array}$$

There is not enough information to solve these equations fully but as the triple unsaturation (T) is the minor component, an estimate of the saturates, monounsaturates and doubly unsaturated components (S, M and D) can be made by setting T to zero. Table 11 shows the results from this analysis for seven oils. Included in the table for comparison are the totals of saturated, mono, doubly and triply unsaturated fatty acids which were measured for these same oils by FAME analysis.

**Table 11**

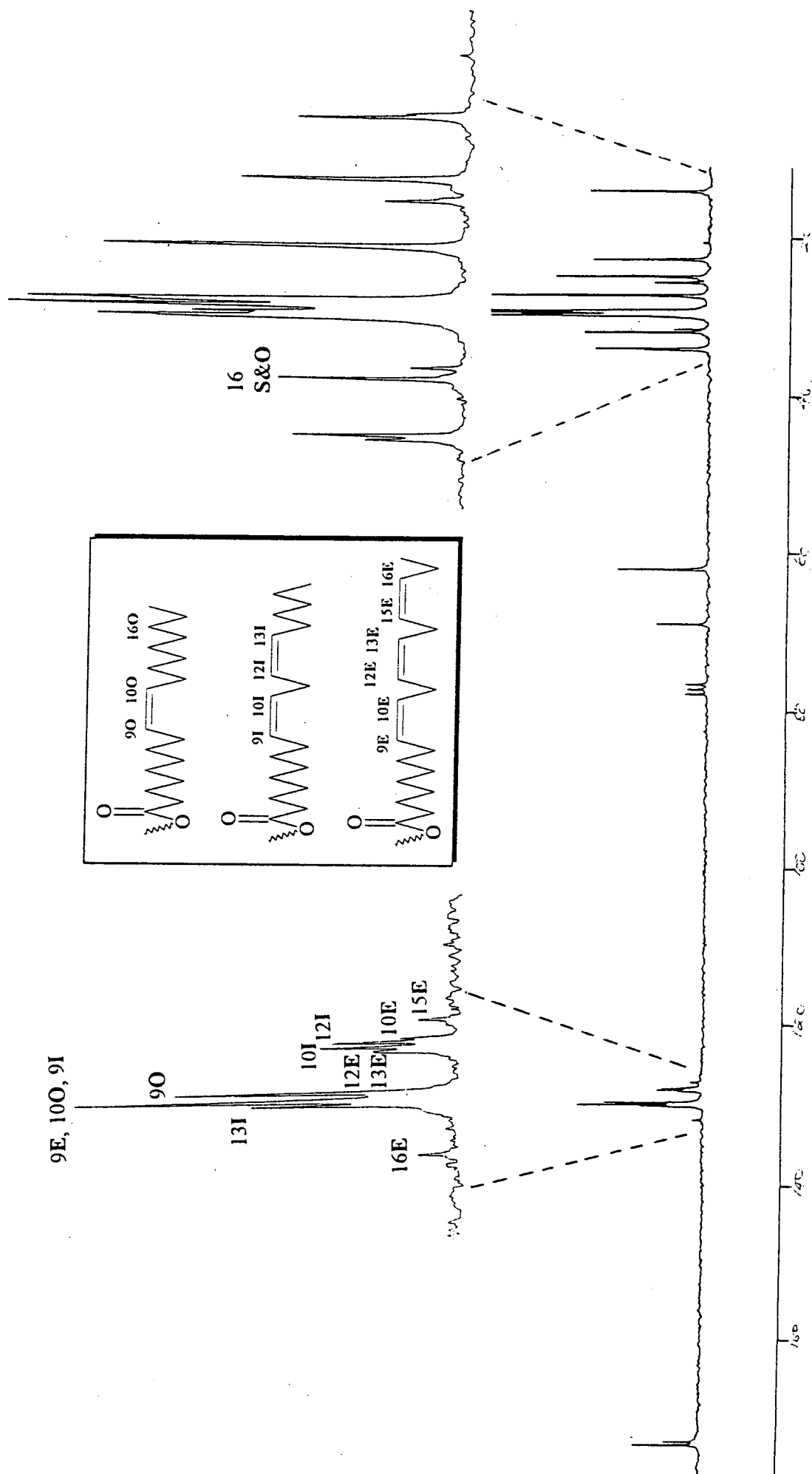
<b><sup>1</sup>H NMR Estimation of % Composition (cf. FAME analysis)</b>				
	<b>Saturated</b>	<b>Mono- unsaturated</b>	<b>Doubly- unsaturated</b>	<b>Triply- unsaturated</b>
	<b>(S)</b>	<b>(M)</b>	<b>(D)</b>	<b>(T)</b>
<b>Grapeseed</b>	6 (10)	27 (16)	66 (74)	zero (0.6)
<b>Groundnut</b>	20 (17)	47 (42)	33 (38)	zero (2)
<b>Olive</b>	19 (13)	69 (78)	11 (9)	zero (0)
<b>Palm</b>	47 (42)	41 (45)	12 (12)	zero (0.2)
<b>Rape</b>	9 (7)	54 (55)	37 (23)	zero (9)
<b>Sesame</b>	20 (15)	40 (39)	40 (46)	zero (0.4)
<b>Soya</b>	17 (14)	25 (23)	58 (53)	zero (7)
<b>Sunflower</b>	15 (13)	28 (23)	57 (63)	zero (0)

The estimated values are generally within 9% of those found by GC analysis. Rape seed oil is an exception as it contains 9% of linolenic acid (18:3) which is not taken into account in the calculation.

## (ii) $^{13}\text{C}$ NMR Analysis

Profiling by  $^{13}\text{C}$  NMR is a more established technique which has been used to gain information on the composition and positional distribution of fatty acids in fats. Gunstone<sup>186</sup> has used high resolution  $^{13}\text{C}$  NMR spectroscopy to identify butterfat, lauric oils, partially hydrogenated fats, linoleic and linolenic acid components in commercially available edible products. He has also applied these techniques to the study of fish oil<sup>187</sup> and hydrogenated fat compositions.<sup>188</sup> Wollenberg used the carbonyl region in conjunction with the alkene signals to examine the acyl positional distributions of several oils: corn, peanut, canola (edible rape seed oil) and high oleic sunflower<sup>189</sup> while Ng concentrated on the carbonyl region to examine fatty acid distribution in palm oil.<sup>190</sup> This technique gives valuable information on the distribution of the acyl groups on the glycerol backbone which would otherwise be determined by hydrolysis of the triglycerides using pancreatic lipase. This enzymatic method removes the 1 and 3 position acyl groups to leave a 2-monoglyceride. Wollenberg's approach, however, requires long periods of NMR instrument time for data acquisition in order to obtain quantitative peak sizes. For example, the alkene spectral region requires about eleven hours for 1000 scans and the carbonyl region approximately half that time.

In this work, authentic spectra of methyl stearate, oleate, linoleate and linolenate were overlaid and compared with published literature examples,<sup>186-192</sup> in order to identify characteristic, well-resolved signals which could be used to quantify the fatty acid compositions of several oil samples. Spectrum 9 shows the  $^{13}\text{C}$  NMR spectrum of rape seed oil, as an illustration, with the peaks which were selected for measurement. These are: C-9 in oleic acid, C-10 in linoleic acid and C-15 in linolenic acid. Their chemical shift values are given in Table 12 along with those of the overlapping oleic and stearic acid C-16 signals. The intensity of this signal is used as a measure of the saturated



Spectrum 9: Rape Seed Oil  $^{13}\text{C}$  NMR (50 MHz)

fatty acids present after subtraction of the estimated oleic acid content (from the C-9 peak).

**Table 12**

Measure of:	M	D	T	S + M
Position in carbon	C(9)	C(10)	C(15)	C(16)
chain chosen:	oleic	linoleic	linolenic	stearic + oleic
Shift value (ppm)	129.17 - 129.35	127.64 - 129.35	ca 126.7	31.5 - 31.6

In order to reduce the data acquisition time for these experiments, a relaxation agent  $[\text{Cr}(\text{acac})_3]$  was added to the oil samples to allow quantitative comparison of  $\text{CH}$ ,  $\text{CH}_2$  and  $\text{CH}_3$  signals. Seven oils were analysed by this method and their compositions are tabulated below, with FAME GC analysis data included in brackets for comparison (Table 13).

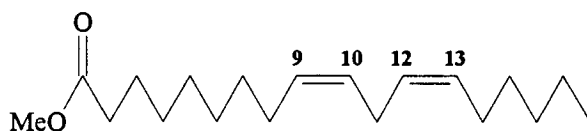
**Table 13**

% Composition by $^{13}\text{C}$ NMR Estimation ( <i>cf.</i> FAME analysis)				
	Saturated	Mono-unsat.	Doubly-unsat.	Triply-unsat.
Grapeseed	10 (10)	16 (16)	73 (74)	nd (0.6)
Groundnut	20 (17)	48 (42)	32 (38)	nd (2)
Palm	48 (42)	44 (45)	8 (12)	nd (0.2)
Rape	12 (7)	57 (55)	23 (23)	7 (9)
Sesame	17 (15)	42 (39)	41 (46)	nd (0.4)
Soya	15 (14)	24 (23)	55 (53)	5 (7)
Sunflower	9 (13)	27 (23)	64 (63)	nd (0)

This method is more accurate and informative than  $^1\text{H}$  NMR estimation (as data for the triply unsaturated components, **T**, is included). It is also rapid and requires no derivitisation of the sample while providing a good estimate of the oil composition in comparison with FAME analysis.

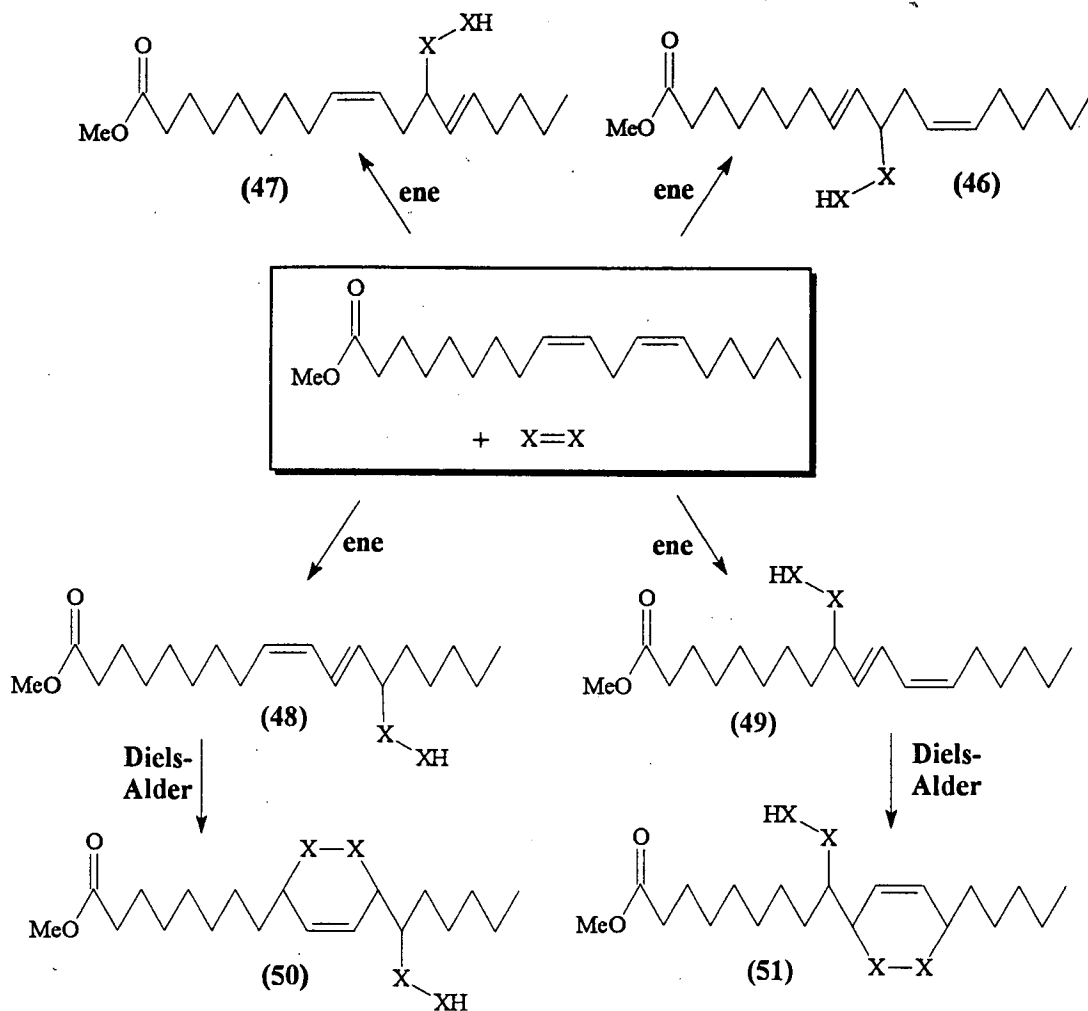
### 3.2 Ene Additions to Vegetable Oils

Vegetable oils are a complex mixture of triglycerides and contain saturated, mono-unsaturated and polyunsaturated acid components (eg. 18:0, 18:1 and 18:2), as described in the previous section (3.1) on their structure and compositional analysis. All the model studies on methyl oleate which were used in the analysis of the jojoba adducts are equally applicable to triglyceride modifications. Many oils, however, contain appreciable amounts of linoleic acid (18:2) in their fatty acid portions; for example sunflower and safflower contain *ca.* 60% and 80% 18:2 respectively. Methyl linoleate (45) was therefore chosen to help in the investigation into ene additions on these methylene interrupted diene fatty acids.



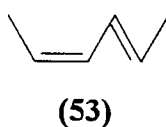
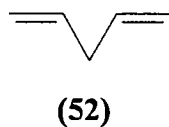
(45)

It can be envisaged that ene addition to such a diene could result in the formation of several products depending on the position of attack of the enophile (and the resultant double bond migration). For example, attachment of an enophile at positions 10 or 12 would lead to an 8,12 or 9,13 diene (46 or 47 in Scheme 53). In contrast, if the enophile attacks at either of the outside positions (9 or 13) a conjugated diene is expected to be formed (48 or 49). Furthermore, if the enophile present is also able to act as a dienophile, movement of the double bonds into conjugation would allow a Diels-Alder cycloaddition to take place to form adducts such as (50 and 51, Scheme 53).



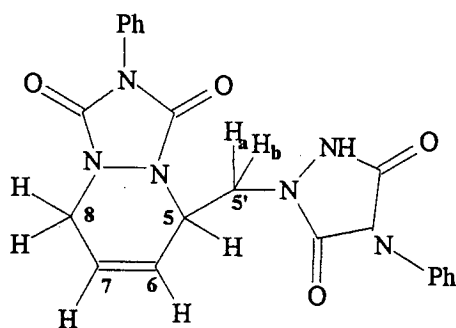
Scheme 53

Before examining methyl linoleate, preliminary experiments were carried out on 1,4-pentadiene (52) and *cis*-2-, *trans*-4-hexadiene (53). The pentadiene mimics the central methylene interrupted fragment of methyl linoleate and the hexadiene models the anticipated diene unit of the initial ene adduct where the new *trans* double bond has been formed in conjugation with the existing *cis* one [(48 and 49), Scheme 53].



### 3.2.1 PTAD as Enophile with 1,4-Pentadiene

A three-fold excess of pentadiene was stirred with PTAD in dichloromethane at 0°C. After two hours the solution had not fully decolourised and so stirring was continued overnight to produce a colourless solution. The solvent and excess pentadiene were removed under vacuum to furnish a white solid in excellent yield (93%). TLC showed the presence of only one product which was highly polar (silica/EtOAc,  $R_f = 0.4$ ). Attempts to recrystallise the product were unsuccessful and so it was examined in its crude state. An accurate mass measurement was obtained which indicated that two moles of PTAD had reacted with each mole of pentadiene to form a diadduct. Its structure was assigned as (54) on the basis of its  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra. This is the result of a tandem ene/Diels-Alder reaction similar to that in Scheme 53 where the ene reaction shifts the double bonds into conjugation and a Diels-Alder cycloaddition subsequently takes place.



(54)

The two methylene carbons (C-5' and C-8) appear at 44.35 and 46.88 ppm with C-5 at a slightly higher shift of 50.89 ppm. The alkene carbons were found at 122.06 and 123.29 ppm, distinct from the strong aromatic absorptions. Finally there were four carbonyl signals at 151.59, 152.75, 153.48 and 153.68 ppm; the latter two are closer in chemical shift and are therefore assigned to the ring-fused PTAD derivative rather than the urazole ring substituent in which the carbonyls are in different environments.

In the  $^1\text{H}$  NMR spectrum, the peaks were generally well resolved with the exception of the two methylenes (8-H and 5'-H) which gave rise to overlapping signals. However, by carrying out decoupling experiments all the peaks were assigned and coupling constants extracted. These are displayed in Table 14.

Table 14

H	$^1\text{H}/\text{ppm, m}$ (360 MHz)	$J_{x,y}/\text{Hz}$	
5'a	3.97 <sup>a</sup>	5'a,5	7.2
5'b	3.60, dd	5'b,5'a	15.1
		5'b,5	2.6
5	4.83, m	5,6	ca. 4
		5,7	nd
6	5.69, dm	6,7	10.4
		6,8a	ca. 2
		6,8b	ca. 2
7	5.92, dt	7,8a	4.0
		7,8b	ca. 2
8a	4.24, ddd	8a,8b	15.9
8b	3.95 <sup>a</sup>		
Ph	7.23-7.47, m		
NH	8.95, br s		

a: 5'a and 8b overlap

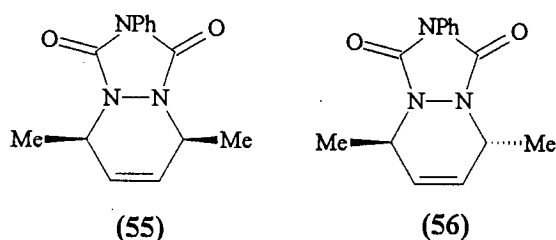
The coupling between the alkene protons is 10.4 Hz which is typical for a six-membered ring. Protons 8a and 8b appear at 4.24 and 3.95 ppm and have different couplings of 4.0 and *ca.* 2 Hz to the adjacent unsaturated proton 7-H. The diastereotopic protons (5a' & b) also have different couplings to the adjacent position (5-H) of 7.2 and 2.6 Hz. The two large couplings of >15Hz for  $\text{H}_{5a}/\text{H}_{5b}$  and  $\text{H}_{8a}/\text{H}_{8b}$  are typical for these geminal relationships.<sup>193</sup>



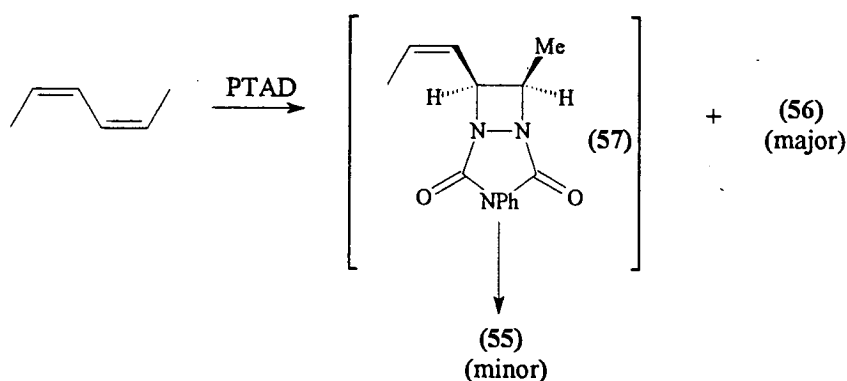
### 3.2.2 PTAD as Enophile with *cis*-2-, *trans*-4-Hexadiene

In Scheme 53 it can be seen that two of the four possible ene addition products (48 and 49) contain a conjugated *cis*, *trans* diene unit. *Cis*-2-, *trans*-4-hexadiene was chosen as a model for this intermediate ene adduct in order to assign the geometry of the final methyl linoleate product and facilitate analysis of its NMR spectra.

Addition of PTAD to the *trans,trans*- and *cis,trans*-2,4-hexadiene isomers in dichloromethane has been investigated by Jensen and Foote<sup>194</sup> who found that both give the expected Diels-Alder products (55 and 56; methyl groups *cis* and *trans* respectively) with high stereospecificity (>200:1).



Addition to the *cis,cis*- isomer, on the other hand, gives a mixture of two Diels-Alder products, with the major isomer having its methyl groups *trans*. The formation of the *trans* product is contrary to that expected for a concerted process but they propose a multi-step mechanism involving a diazetidine intermediate which is consistent with these products (Scheme 54).



Scheme 54

$^{13}\text{C}$  NMR studies have been carried out by Fischer *et al*<sup>195</sup> to determine the conformation of the tetrahydropyridazines derived from *cis*, *cis*-2,4-hexadiene with PTAD and DEAD. More recently a comparative study has been carried out to compare this information with the conformations found in the solid state by crystallography<sup>196</sup>. The *cis*, *trans*-2,4-hexadiene had not, however, been included in these studies and so its conformation both in solution and in the solid state was examined.

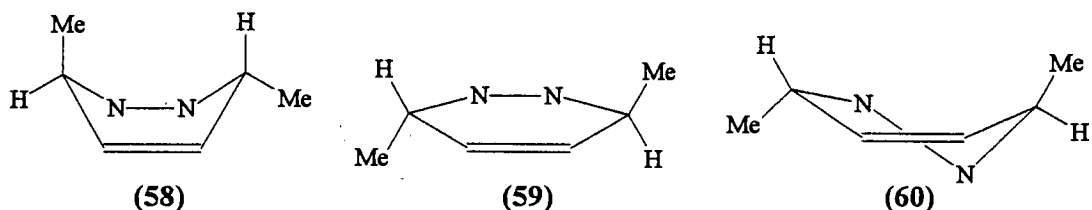
The reaction of of equimolar quantities of PTAD with hexadiene was very rapid, taking 90 s to reach completion at 0°C, and afforded a single adduct in high yield (96%). The adduct was recrystallised from ethanol and gave a satisfactory CHN analysis and melting point with respect to the literature value for the *trans* Diels-Alder adduct (56).<sup>194</sup>

$^1\text{H}$  NMR examination revealed that the two methyl substituents are equivalent and appear as a doublet at 1.30 ppm split with a coupling of 6.5 Hz to the adjacent ring protons. The ring CH protons are seen at 4.54 ppm as a doublet of quartets. They couple to the adjacent methyl groups ( $J$  6.5 Hz) and to the adjacent alkene with a small coupling of  $J$  2.4 Hz. The alkene protons are also equivalent and appear at 5.81 ppm as a doublet, split by the adjacent ring CH ( $J$  2.5 Hz). There is no allylic coupling to the methyl groups.

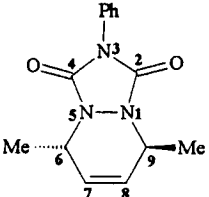
The  $^{13}\text{C}$  NMR spectrum is also a simple picture: the methyl carbons both appear at 16.37 ppm, the ring CHs at 49.81 ppm and alkene carbons at 124.99 ppm. There are also the expected signals for the phenyl ring and one carbonyl absorption at 152.14 ppm.

From the above evidence, the boat-like conformation for this tetrahydropyridazine can be ruled out (58) as it would give several more non-

equivalent signals in the NMR spectra. A planar (59) or half-chair configuration (60) would, however, fit with the observed  $^1\text{H}$  and  $^{13}\text{C}$  NMR signals.



Crystals of the adduct were grown and an X-ray crystal structure of the compound was obtained (Figure 8). This not only confirmed the *trans* arrangement of the methyl groups but also the conformation type predicted (in solution phase by NMR). Furthermore, it gave information on the torsion angles which are consistent with the small coupling constant between the alkene protons and the adjacent CH ring protons. Two broadly similar forms were observed in the crystal lattice; their torsion angles were:

Compound (56)	Torsion Angles:	
	H(9)-C(9)-C(8)-H(8)	H(6)-C(6)-C(7)-H(7)
Crystal form 1	46.6°	44.6°
Crystal form 2	43.0°	48.2°

Used in the Karplus equation ( $^3J_{ab} = J\cos^2\phi - 0.28$  [ $90^\circ \geq \phi \geq 0^\circ$ ]) the predicted coupling constants work out at between 3.5 and 4.2 Hz. These are higher than the observed  $J$  value of 2.5 Hz although the Karplus equation does not take into account the presence of the electronegative nitrogens which will lower the coupling constants.

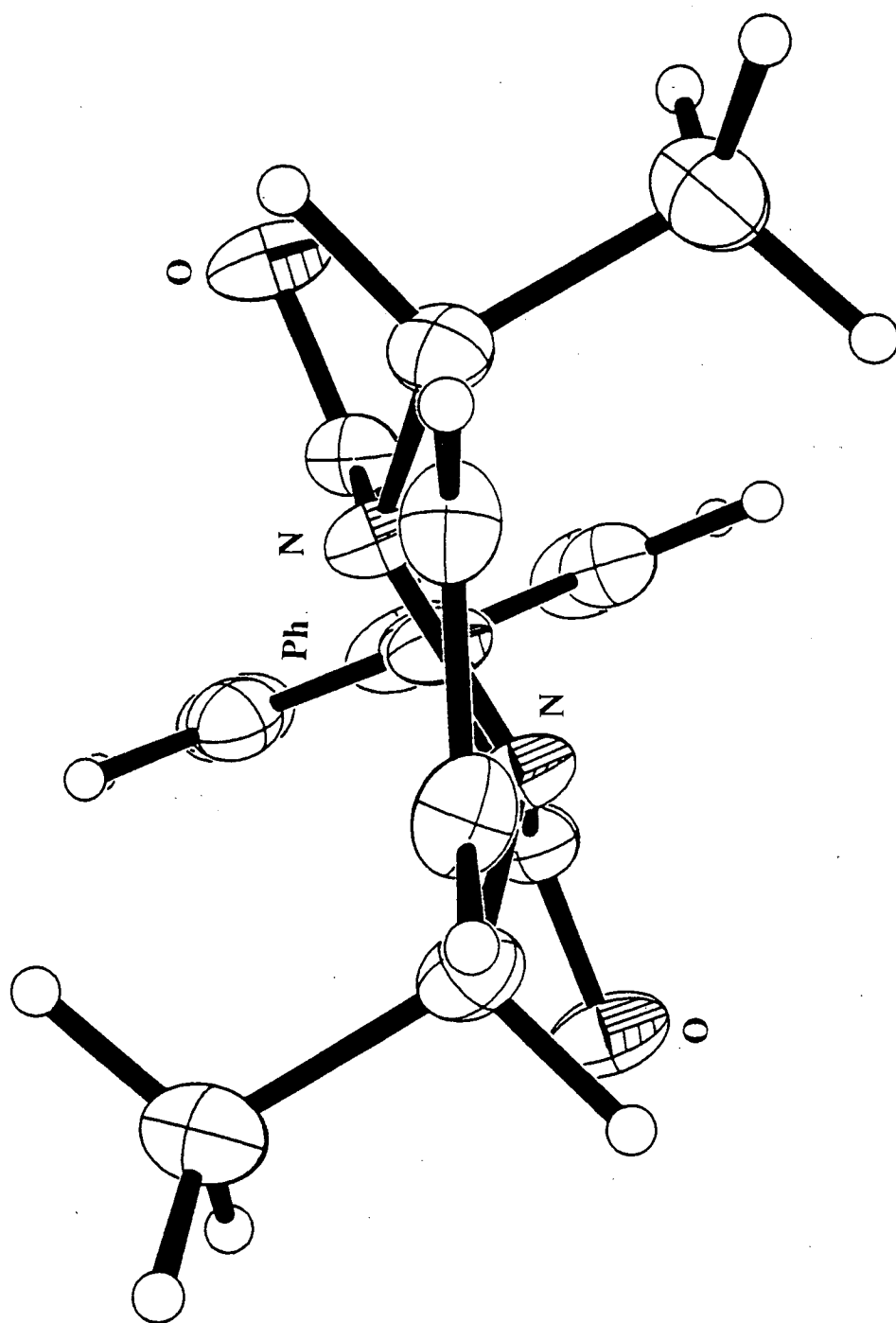
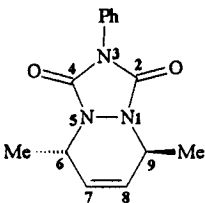
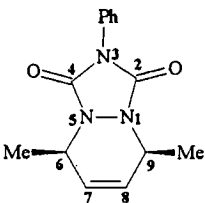


Figure 8: X-ray Crystal Structure of Compound (56)

The X-ray crystal structure also provides information on the arrangement of atoms in the urazole ring. The degree of planarity/pyramidality is measured by averaging the bond angles around nitrogen; an average of 120° corresponding to a planar system while 109° indicates a pyramidal arrangement. The pyramidality at the three nitrogen positions was found to be:

Compound (56)	Pyramidality at:	
	N1	N5
		
Crystal form 1	115°	115°
Crystal form 2	115°	116°
Compound (55)		
		
(Reference 196)	117°	119°

Therefore it can be seen that at the ring junction nitrogen positions the *trans* adduct has a higher degree of pyramidality than the *cis* adduct. These experiments confirm that the *cis-trans* diene unit gives a *trans* adduct and also provide NMR data for the adduct. This is an aid to the analysis of the more complex mixtures formed from methyl linoleate and vegetable oil modifications.

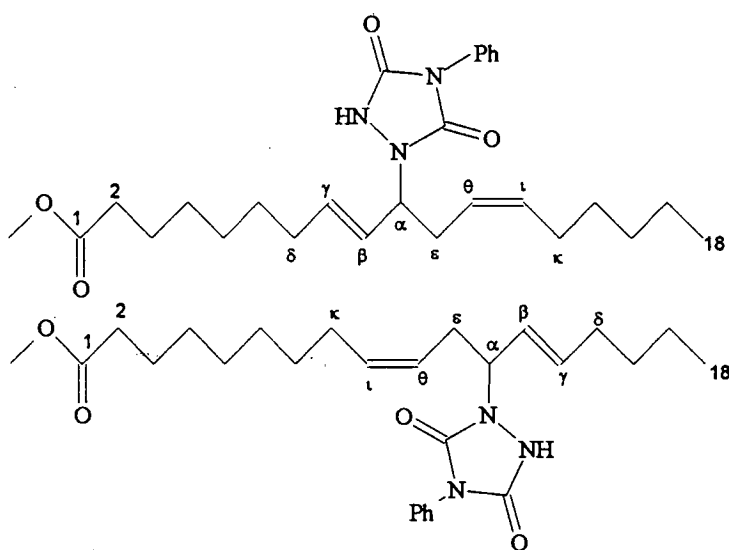
### 3.2.3 PTAD as Enophile with Methyl Linoleate

The reaction of equimolar quantities of methyl linoleate and PTAD was extremely rapid at 0°C. Within 2.5 minutes the bright red colour of the enophile had faded to pale orange. Three fractions were observed by TLC and were separated by dry-flash chromatography in the following order of elution:

- i) recovered methyl linoleate (32%) identified by  $^1\text{H}$  NMR comparison with an authentic sample.
- ii) 1:1 ene adducts (36%) whose spectral characteristics will be discussed in the following paragraphs
- iii) 2:1 tandem ene/Diels-Alder adducts (32%) whose structures were deduced with the aid of NMR decoupling and correlation experiments. These will also be described.

#### ii) 1:1 Adducts

Four isomeric 1:1 adducts can be envisaged in this ene addition as depicted in Scheme 53 (46 - 49). Of the four isomers, two have their double bonds shifted together into conjugation (48 & 49) and the other two (46 & 47) have them moved further apart with the urazole moiety becoming attached between them.



(46 & 47)

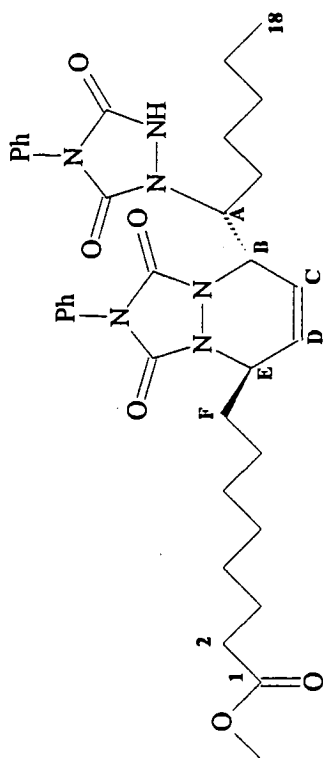
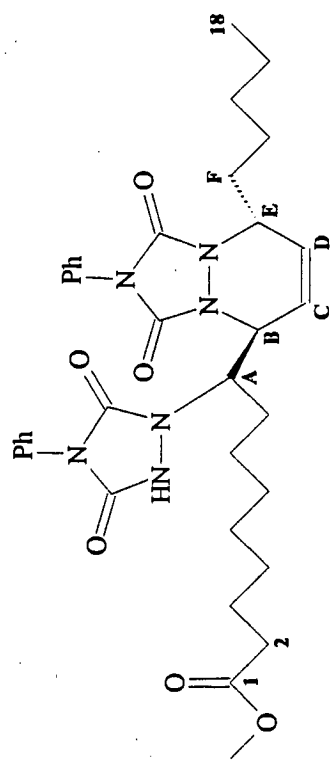


The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra reflect the complexity of this mixture. However, a full assignment has been carried out and is tabulated in Appendix 6. In the  $^1\text{H}$  NMR (Spectrum 10), decoupling experiments were carried out which revealed that the non-conjugated adducts (46 & 47) were the major products. The signal at 2.70 ppm from the inter double bond methylene in the methyl linoleate starting material is totally absent in the product spectrum while the new inter double bond methylene ( $\text{CH}_2\text{-}\epsilon$ ) contained diastereotopic protons ( $\epsilon_A$  and  $\epsilon_B$ ). These produced a complex pattern of two dddd at 2.35 and 2.54 ppm, with a mutual coupling of 15 Hz. Protons  $\epsilon_A$  and  $\epsilon_B$  each coupled differently to the adjacent H- $\theta$  and H- $\alpha$  positions. H- $\beta$  and H- $\gamma$  were *trans* to each other and appeared at similar chemical shifts to H- $\beta$  and H- $\gamma$  in the methyl oleate/PTAD adducts. Protons  $\theta$  and  $\iota$  were assigned as the signals at 5.30 and 5.45 ppm. The coupling between them is 10 Hz which confirms that one of the *cis* double bonds is retained in the adduct. Traces of the conjugated 1:1 adducts (47 & 48) were also identified at a level of *ca.* 10% of the total monoadducts.

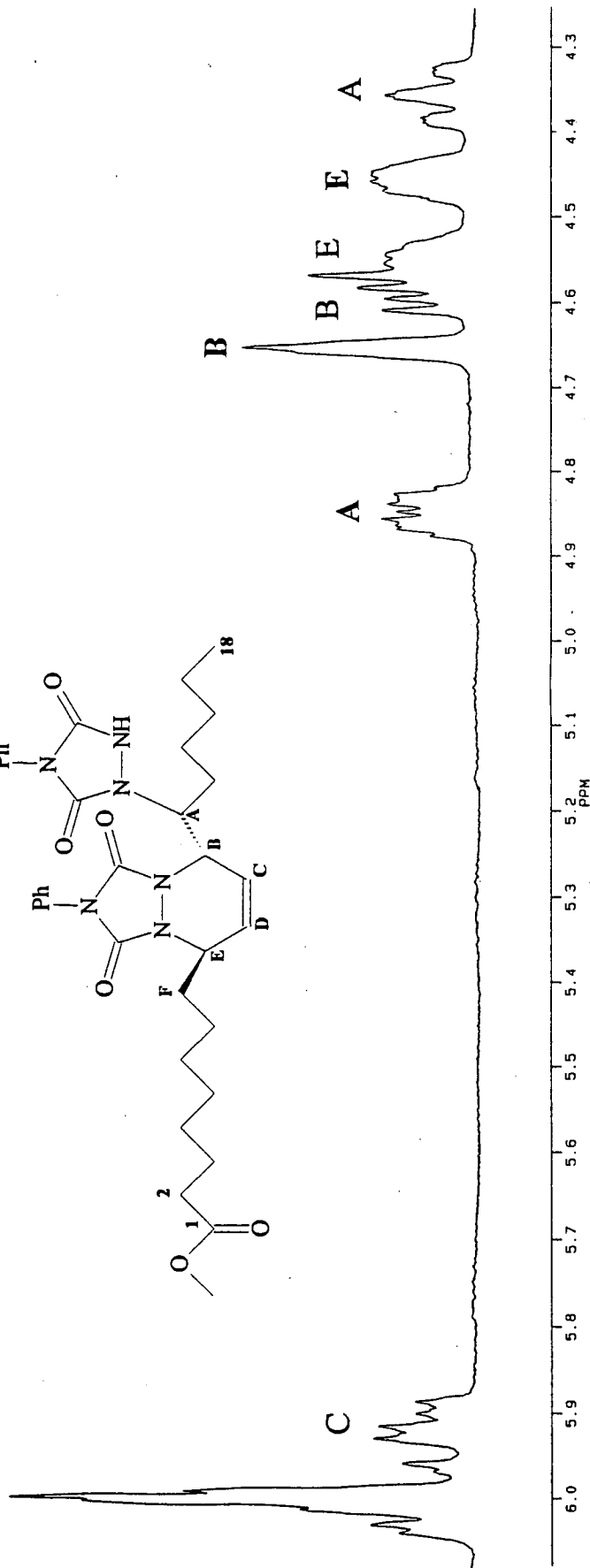
The  $^{13}\text{C}$  NMR not only shows doubling of the carbon signals at C-18, 17 and 16 due to the presence of regioisomers (*ie.* 48 and 49 in Scheme 53) but also confirms that the non-conjugated adducts are the major products and shows evidence of the conjugated products (50 and 51) as minor components.

It is not surprising that there is so little of the conjugated 1:1 adducts remaining when the speed of the model *cis, trans*-2,4-hexadiene reaction is considered. This reaction went to completion in 90 seconds and so it is expected that any conjugated *cis-trans* mono-adduct formed will rapidly undergo a Diels-Alder cycloaddition to form a 2:1 adduct. On the other hand, the non-conjugated monoadduct is not prone to any further additions and so remains in its present form.





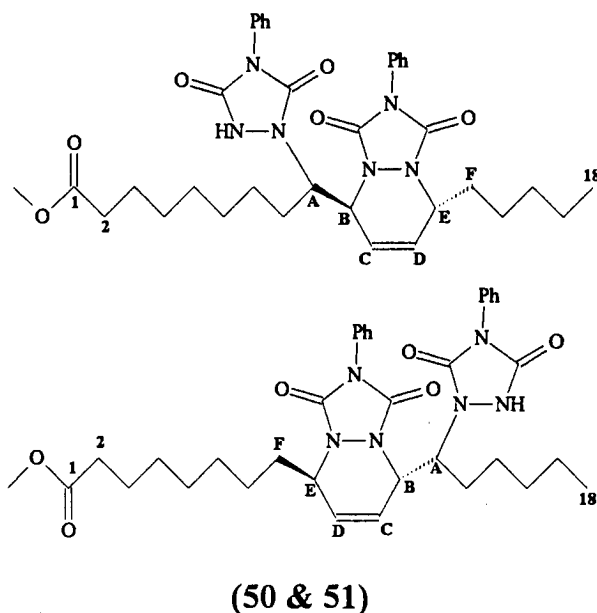
D D C



Spectrum 11: Methyl Linoleate/PTAD Diadducts  
<sup>1</sup>H NMR (360 MHz)

### iii) 2:1 Adducts

The two regioisomers (50 & 51) formed by tandem ene/Diels-Alder addition in Scheme 53 both contain three chiral centres (A, B and E).



The relative stereochemistry of carbons B and E within the ring is fixed by the Diels-Alder cycloaddition while the presence of the adjacent centre at carbon A means that two pairs of diastereomers are likely to be formed. These diastereoisomeric pairs will have differing physical and chemical properties, and this is evident in the  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of the 2:1 adduct fraction. The  $^1\text{H}$  NMR spectrum is shown in Spectrum 11. The region between 4.3 and 4.9 ppm contains six signals, two of which are overlapping. This is in contrast to the 1:1 adducts which contained only one signal in this region; that of the  $\alpha$ -CHN proton. On expansion of these peaks and their integrals it was noted that not all the integrals were equal in size; three were larger (measuring 45 mm in height) while the other three had integrals of 38 mm. This was also reflected in the alkene region where there was one signal at *ca.* 5.9 ppm with an integral of 38 mm while the other absorption at *ca.* 6.0 ppm had an integral composed of 2 x 45 mm plus 1 x 38 mm. With the aid of this information and a COSY experiment, the three protons A, B and E were assigned for each of the two diastereoisomers (Appendix 7).

The  $^{13}\text{C}$  NMR spectrum also reflected the presence of diastereoisomers. It contains six distinct signals (53.6 - 56.9 ppm) for the two sets of CH carbons (A, B and E). Two alkene signals are seen at 119.10 and 121.76 ppm and two more would be expected but these are concealed by the strong phenyl absorptions between 125 and 131 ppm. Assignments are given in Appendix 7. In related work in Edinburgh,<sup>197</sup> on the use of MTAD with methyl linoleate, these extra sets of alkene signals were observed.

In summary, the reaction of PTAD with methyl linoleate resulted in the formation of approximately equal quantities of conjugated and non-conjugated dienes. The conjugated adducts could not be isolated and were only observed in trace amounts as they were highly susceptible to further reaction with PTAD as a dienophile to furnish tandem ene/Diels-Alder diadducts as diastereoisomeric pairs.

#### 3.2.4 MTAD as Enophile with Methyl Linoleate

As mentioned in the previous section (3.2.3) MTAD was reacted with methyl linoleate as part of a related honours project.<sup>197</sup> It was noted that the distribution of conjugated : non-conjugated diene : tandem diadduct was different from that of the PTAD enophile. In order to further investigate this observation, several reactivity comparisons with the two triazolines were carried out at 0°C, involving not only methyl linoleate but also the model compounds *cis,trans*-2,4-hexadiene and 1,4-pentadiene.

A dramatic difference between the dienophilicity of the MTAD and PTAD was observed with the hexadiene; while an equimolar ratio of PTAD was decolourised within 20 s with hexadiene, the equivalent reaction with MTAD had still not totally decolourised after 18 hours. 1,4-Pentadiene also reacted faster with PTAD than with MTAD.

In the case of methyl linoleate, the MTAD had faded to colourless within 21 minutes while the equivalent PTAD reaction was complete within 4 minutes. Examination of the crude MTAD reaction products by  $^1\text{H}$  NMR revealed that the conjugated and non-conjugated ene adducts had been formed as well as the tandem diadduct. By integral expansion of selected peaks, the ratio of products was estimated as 1.5 : 3 : 2 respectively with *ca.* 35% unreacted methyl linoleate also present. In the PTAD case there was more tandem diadduct formation and only traces of the conjugated mono-adducts observed. This is in accordance with the reduced Diels-Alder reactivity found with hexadiene. This can be rationalised by the change in triazolinedione substituent from phenyl to methyl. Diels-Alder cycloadditions are favoured by electron-rich dienes and electron-poor dienophiles. The methyl substituent on triazolinedione is weakly electron-donating and therefore will induce a lower dienophilicity than the phenyl group which can conjugatively withdraw electrons from the triazoline ring to accelerate the reaction.

### 3.2.5 DEAD as Enophile with Methyl Linoleate

The final azo enophile reacted with methyl linoleate was DEAD. This addition was carried out at two different ratios by refluxing the ene and enophile together in 1,1,1-trichloroethane (as detailed in Table 15).

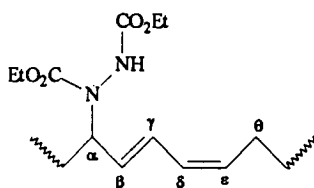
Table 15

Reactant Ratios		Reaction Time	Product Yields			
methyl linoleate	DEAD		recovered alkene	1:1 ene adducts (61)	tandem ene/D-A (62)	other 2:1 adducts
0.592 g 2.0 mmol	0.348 g, 2.0 mmol	48 h	13%	67%	4%	7%
0.294 g 1.0 mmol	0.348 g 2.0 mmol	120 h	trace	38%	16%	20%

As with previous enophiles, both mono and di-adducts were isolated by chromatography and their identities confirmed by accurate mass measurement. Methyl linoleate was also recovered from the first reaction mixture although examination by  $^{13}\text{C}$  NMR showed that the allylic and doubly-allylic signals had reduced in size while signals had appeared at *ca.* 32 ppm. This suggests that the methyl linoleate had undergone partial isomerisation during the reaction or work up. A sample of methyl linoleate was therefore refluxed in 1,1,1-trichloroethane and examined periodically by  $^{13}\text{C}$  NMR to monitor for isomerisation at this temperature. After 80 hours there was no sign of any alterations and so it is concluded that it was not temperature alone which had caused the starting methyl linoleate to isomerise.

The major products from this addition were 1:1 adducts. The  $^1\text{H}$  NMR spectrum was consistent with the conjugated diene products rather than the non-conjugated ene adducts. These would produce distinctly different splittings in the alkene region. A full assignment is tabulated in Appendix 11 for both  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra. The alkene protons  $\alpha, \beta, \gamma$  and  $\epsilon$  are clearly resolved and contain the expected splittings for a *cis,trans* conjugated diene as detailed below in Table 16.

Table 16



(61)

Proton	$\alpha$	$\beta$	$\gamma$	$\delta$	$\epsilon$
$\delta$ /ppm	4.59	5.56	6.40	5.90	5.40, 5.43
m	m	dd	dd	t	2 x dt
$J(xy)$ /Hz	-	$\beta\gamma$ 15.1 $\beta\alpha$ 7.8	$\gamma\beta$ 15.0 $\gamma\delta$ 11.3	$\delta\epsilon, \delta\gamma$ <i>ca.</i> 11.0	$\epsilon\delta$ 10.0 $\epsilon\theta$ 7.2

Despite careful examination of the fractions from the column, no non-conjugated diene adduct was observed in the reaction mixture. A rationale behind this is that as the reaction is very much slower than in the triazolinedione case, it may also be more selective and the enophile may only be adding to the two external positions in methyl linoleate and abstracting a proton from the doubly-allylic methylene position. This would selectively produce the conjugated diene monoadduct.

Smaller amounts of more polar compounds were isolated from the mixture. An accurate mass measurement showed that the first of these fractions was consistent with a diadduct. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were broad and could not be fully assigned. However, the absence of an allylic methylene signal at *ca.* 2 ppm allowed this fraction to be tentatively assigned as a tandem ene/Diels-Alder diadduct analogous to those found with PTAD and MTAD. Finally, the second of the more polar fractions was examined by NMR but it also gave extremely broad signals which could not be assigned, although the spectra were distinct from those of the suspected tandem diadduct. This fraction was therefore not identified but could be a result of a second ene addition to the 1:1 ene adducts.

### 3.2.6 Formaldehyde as Enophile with Methyl Linoleate

Methyl linoleate was reacted with a 2.2 times excess of formaldehyde at 0°C using EtAlCl<sub>2</sub> as the catalyst. The reaction was quenched with ether and worked up as before. Chromatography was carried out in order to purify the reaction products. Methyl linoleate (39%) was recovered and examined by <sup>13</sup>C NMR. The recovered alkene had undergone partial isomerisation as indicated by the reduced intensities of the allylic and doubly-allylic signals. The major products were isolated in 46% yield and their accurate mass measurements corresponded to a dehydrated fragment of the monoadducts. There was no indication that the monoadducts had undergone dehydration in the NMR spectra and the FTIR spectrum showed a broad absorption at 3450 cm<sup>-1</sup> (OH). It is concluded that the fragmentation apparent in the mass spectrum is caused by the FAB mass spectroscopy conditions. Examination by <sup>1</sup>H NMR at field strengths of 360 and 600 MHz (Spectrum 12) indicated that the monoadducts were non-conjugated dienes (63A & B).

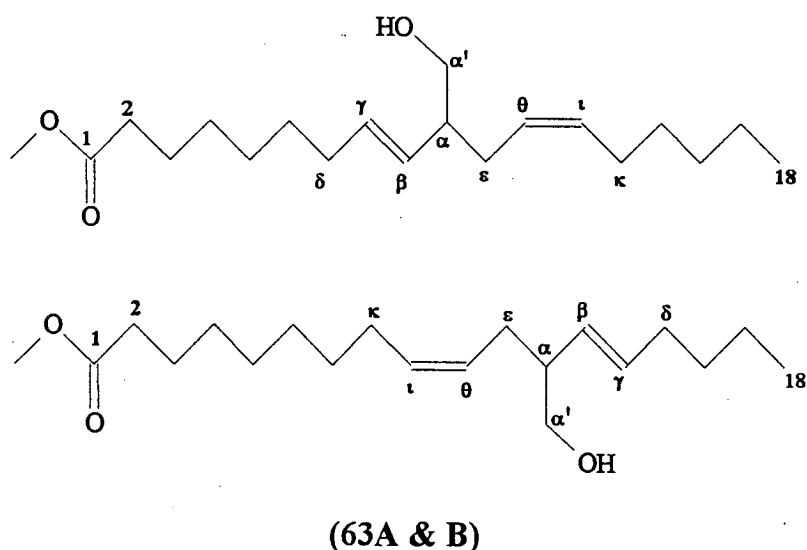
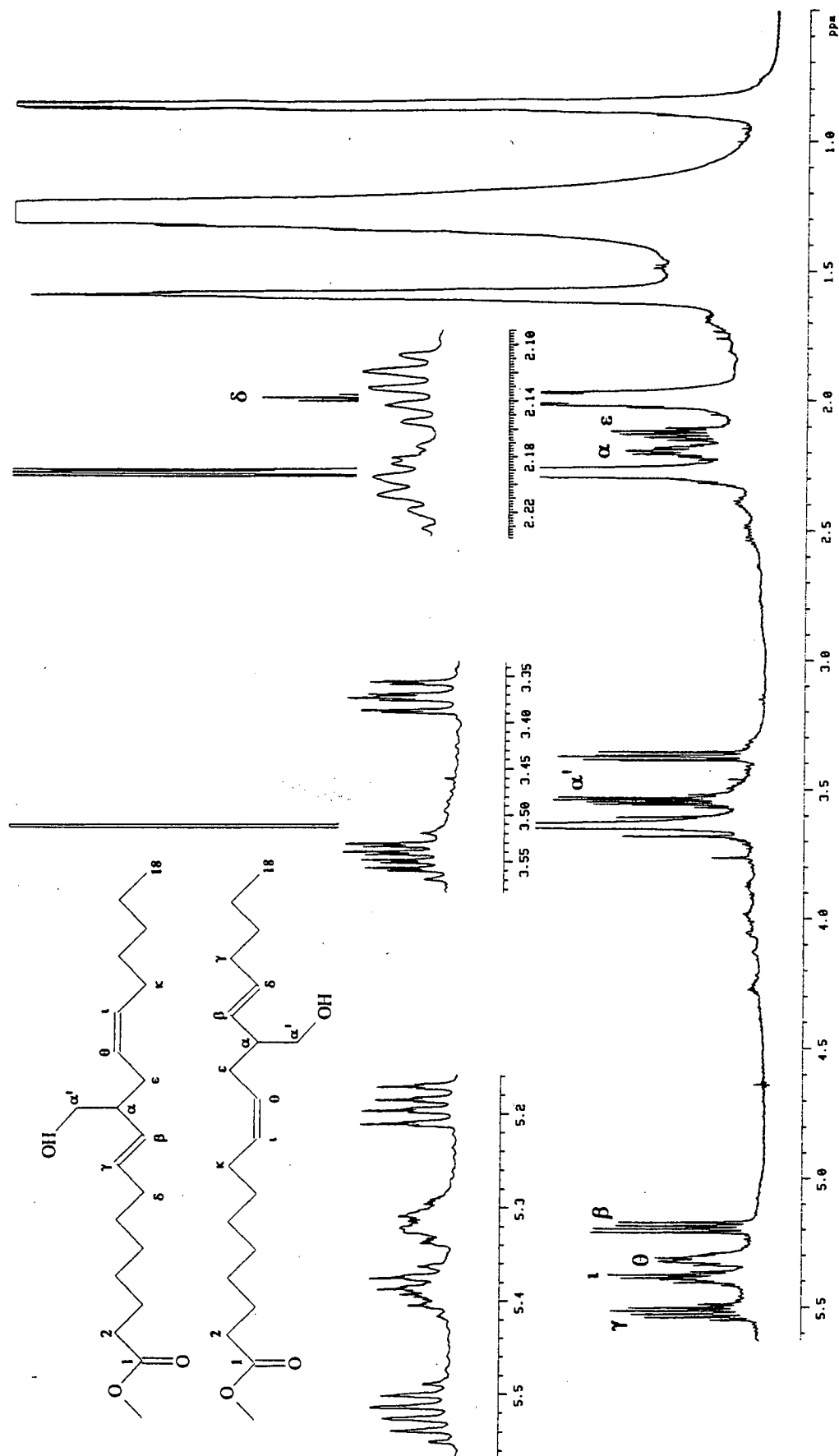


Table 17 shows the <sup>1</sup>H NMR assignment for the alkene signals and those of the adjacent positions in compound (63).



Spectrum 12: Methyl Linoleate/Formaldehyde Monoadducts  
 $^1\text{H}$  NMR (600 MHz)

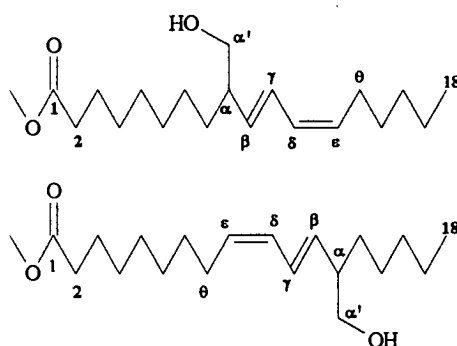


Table 17

Proton	$\alpha$	$\beta$	$\gamma$	$\delta$	$\epsilon$	$\theta$	$\iota$
$\delta/\text{ppm}$	2.20	5.19	5.51, 5.54	1.99, 2.02	2.13	5.32	5.39, 5.40
m	m	ddt	2 x dtd	2 x q	m	m	2 x ddt
$J/\text{Hz}$	-	15.3, 8.4, 1.5	15.3, 7.9, 0.9	7.3	-	-	10.9, 7.1, 1.5

At this field strength, doubling of the alkene signals is visible in the  $^1\text{H}$  NMR spectrum as there are two regioisomers present (63A&B). The diastereoisomeric protons  $\alpha'_\text{A}$  and  $\alpha'_\text{B}$  also display doubling as a consequence; in this case the centres of each of the two doubled patterns are only separated by 0.002 - 0.003 ppm but are nevertheless still resolved at 600 MHz. Their couplings contain a mutual splitting of 10.5 Hz (geminal) as well as different splittings to  $\alpha$ -H of 7.9 and 5.2 Hz. In the  $^{13}\text{C}$  NMR spectrum (at 50 MHz), doubling of positions C-18 and C-17 is noticable. Furthermore, the alkene and allylic positions  $\beta, \gamma, \delta, \theta$  and  $\iota$  also demonstrate doubling. C- $\alpha$  appears at 45.54 ppm and C- $\alpha'$  at 65.36 ppm.

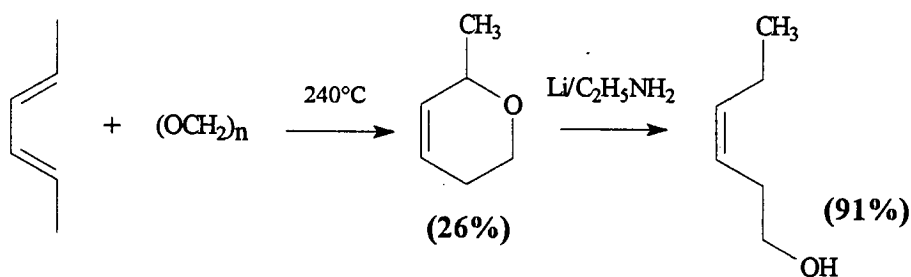
At 360 MHz, traces of another product are visible. There is a small triplet at 5.95 ppm ( $J$  11 Hz) and a doublet of doublets at 6.37 ppm ( $J$  15 and 11 Hz). These are attributed to traces of the conjugated diene adduct 64A&B (H- $\delta$  and H- $\gamma$  respectively).



(64A&amp;B)

By integral expansion, the quantity of the conjugated diene was estimated at *ca.* 10% of the total monoadducts (*ie. ca.* 4% of the total products formed). At 600 MHz these extra peaks were not resolved.

A small quantity (*ca.* 8%) of more polar material was isolated from the column in the search for a tandem ene/Diels-Alder 2:1 adduct but neither the  $^1\text{H}$  NMR spectrum nor the mass spectrum showed any evidence for the diadduct. In the past, formaldehyde has been used as a dienophile in the high temperature synthesis of *cis*-3-hexenol from 1,3-pentadiene and paraformaldehyde (Scheme 54).<sup>198</sup>



Scheme 54

In summary, four enophiles were reacted with methyl linoleate and the percentage yield of each adduct type is shown in the table below.

Table 18

Enophile	enophile:					
	ene ratio	alkene	non-conj. 1:1 adduct	conj. 1:1 adduct	tandem ene/D-A diadduct	double ene diadduct ?
PTAD	1:1	32%	32%	4%	32%	-
MTAD	1:1	35%	30%	15%	20%	-
DEAD	1:1	13%	-	67%	4%	7%
DEAD	2:1	-	-	38%	16%	20%
CH <sub>2</sub> O	2.2:1	39%	42%	4%	-	-

### 3.2.7 Modification of Vegetable Oils

Sunflower oil was chosen as the ene component for this series of experiments as it has a significant diene fatty acid content, contains mono-unsaturates and saturates, and is low in trienes. A comparison between its compositional analysis by FAME and  $^{13}\text{C}$  NMR profiling is shown below in Table 19. The two methods give similar results.

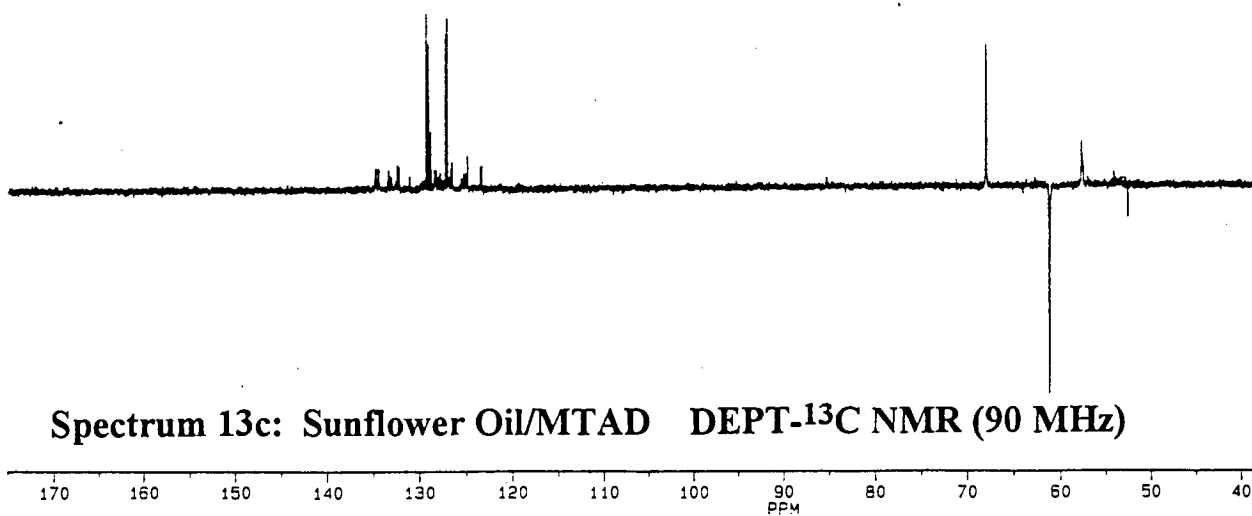
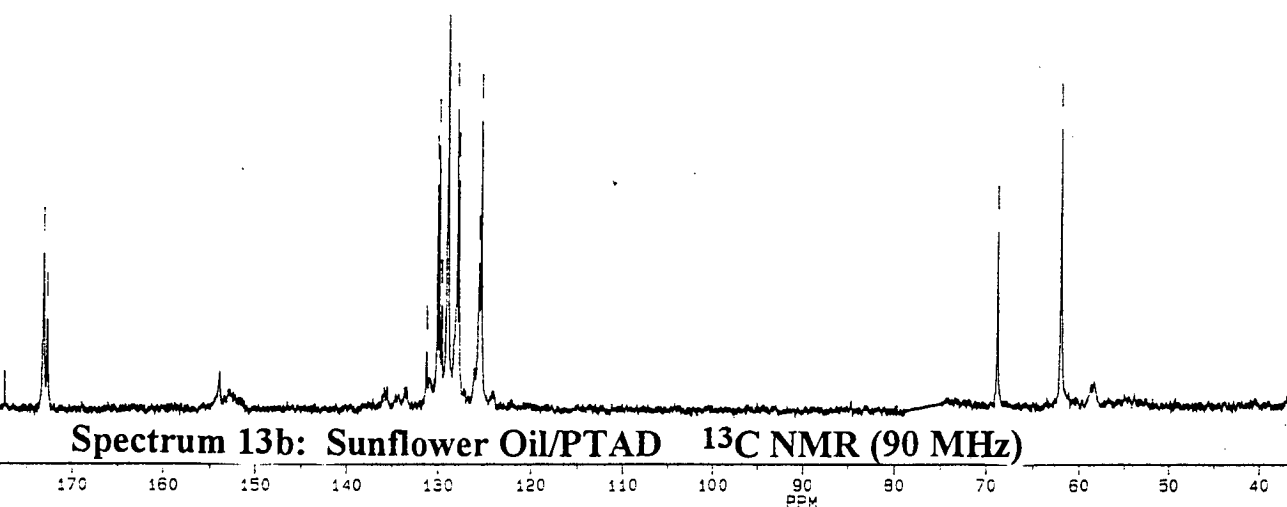
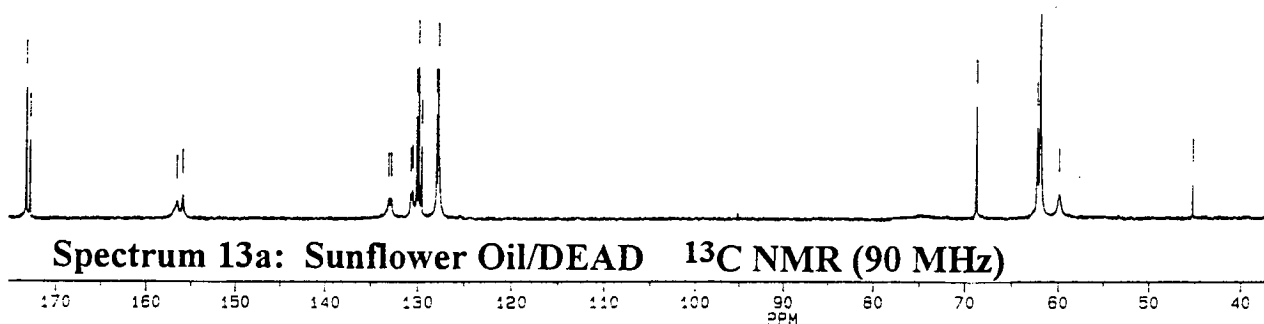
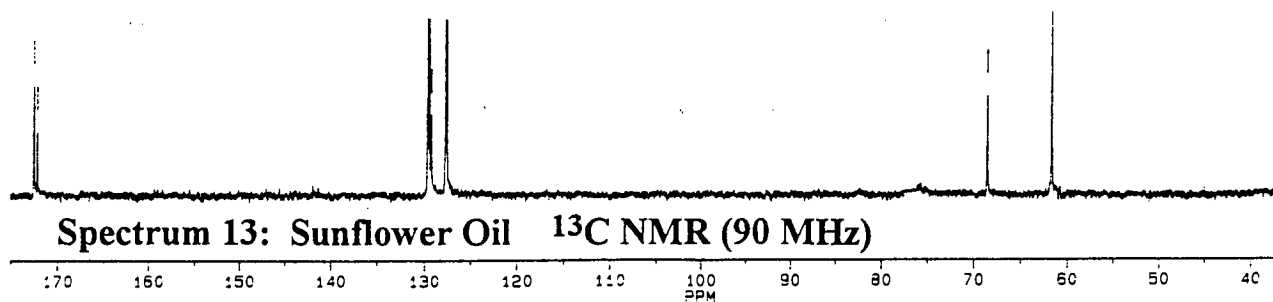
Table 19

Method of analysis:	Number of double bonds per fatty acid:			
	:0	:1	:2	:3
$^{13}\text{C}$ NMR	9%	25%	66%	n.d.
FAME GC	12%	19%	69%	0.2

n.d. - not detected

Using these figures, the average number of double bonds per oil molecule was calculated. From the FAME gas chromatography analysis the equivalent number of double bonds per molecule was 4.8 while from the  $^{13}\text{C}$  NMR method, it was 4.7.

Three enophiles were used to modify the sunflower oil; DEAD, PTAD and MTAD. In order to ensure that all the enophile was consumed in each reaction, the number of double bonds in the oil was kept at approximately three times in excess over the number of moles of each enophile (*ie.* 1.2 mmol of sunflower oil was reacted with 1.89 mmol of each enophile). The PTAD and MTAD reactions were carried out in dichloromethane at  $0^\circ\text{C}$  and went to completion in 15 minutes while the DEAD addition took place in refluxing 1,1,1-trichloroethane over 48 hours. The resultant mixtures were examined without purification by  $^{13}\text{C}$  NMR spectroscopy (using wide-bore 10 mm sample tubes for better sensitivity without having to use an excessive number



of scans) and compared with the  $^{13}\text{C}$  NMR spectra of the model adducts from methyl oleate and methyl linoleate.

Spectrum 13 shows unreacted sunflower oil (40 - 175 ppm), Spectra 13a, b and c show the same region after reaction with DEAD, MTAD and PTAD respectively. In each spectrum the residual unreacted alkene signals show strong absorptions. Smaller signals from the reaction products are also visible.

After DEAD addition, five new signals appear at 127.6, 130.5, 130.7, 132.7 and 133.0 ppm (Spectrum 13a). By comparison with model spectra these peaks are assigned as from a conjugated diene adduct, resulting from addition to a linoleate-type fatty acid component. The expected peaks for an oleate-type ene adduct (at 127 and 133 ppm) may be present but are masked by diene adduct signals. There was no detection of tandem ene/Diels-Alder 2:1 adducts in the 50 - 60 ppm region.

Spectrum 13b shows that on addition of PTAD to sunflower oil, the non-conjugated diene adduct is the major product, while the conjugated diene is also formed. Peaks are also assigned to the ene adduct of the monounsaturated oil component. The region in which tandem ene/Diels-Alder diadduct peaks would be expected (118 - 122 ppm) does not contain any strong absorptions at this level of modification, although as the signal:noise ratio is low, these peaks could be hidden. Indeed, in the region 52 - 58 ppm there is a suggestion of the presence of peaks which would be expected for the tandem diadduct.

Spectrum 13c shows a region of the  $^{13}\text{C}$  NMR spectrum of the crude MTAD modified sunflower oil. A complicated picture is evident and peaks with similar intensities, resulting from both conjugated and non-conjugated diene adducts can be assigned. The presence of smaller amounts of the mono-

unsaturated ene adduct is also detected. Although the signal:noise ratio in this spectrum is better than in the PTAD experiment, at this level of modification there are no peaks detected corresponding to the tandem diadduct. Neither are there any signs of other tandem diadduct peaks at lower shift values (in an expansion of the region 56 - 58.5 ppm).

Although these observations have generally been based on the alkene signals for each adduct type, the peaks resulting from the carbon atoms where the enophiles became attached (usually denoted by  $\alpha$ -CH) were also examined. These absorptions are in the region 52 - 60 ppm but it is less clear which peaks can be assigned to which adduct type. The tandem ene/Diels-Alder diadduct gives rise to up to six absorptions in this region and these can often coincide with the monoadduct signals thus complicating assignments. This region has, however, been of value as confirmation of the assignments made by analysis of the alkene regions.

An alternative approach was also adopted in an attempt to quantify the sunflower oil adducts formed; using gas chromatography. The methyl oleate/PTAD monoadducts and the mono and diadducts from methyl linoleate/PTAD were separated with acceptable resolution at Castrol. Having achieved this separation, the vegetable oil adducts were transesterified to form their methyl esters before being injected onto the same column. Unfortunately the adducts had degraded, presumably during the methanolysis step, and so could not be quantified.

## 4. SYNTHETIC FLUIDS

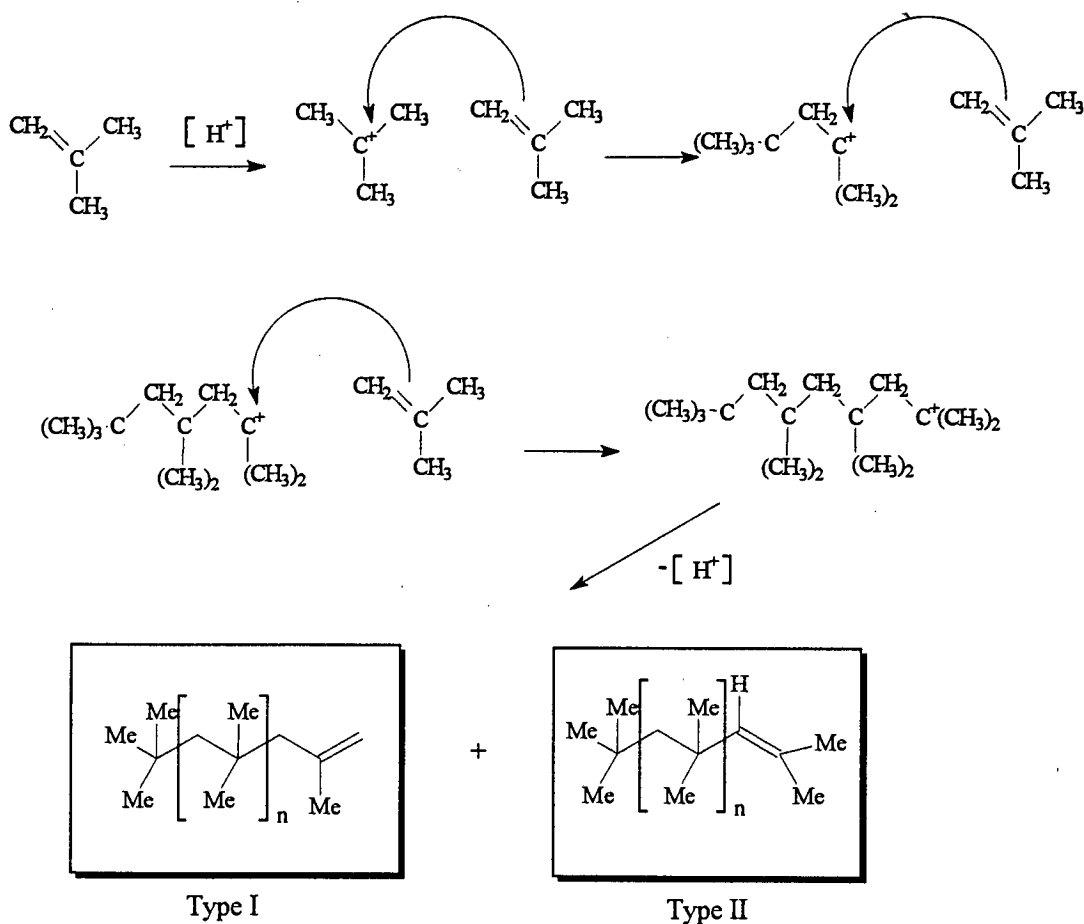
### 4.1 Introduction

The aim of this section of work was to modify two types of commercially important polymers (polyisobutenes and polyalphaolefins) which are used as dispersants and basestocks respectively in the formulation of synthetic lubricants. As these polymers are non-polar their presence in lubricant packages can lead to additive solubility problems.<sup>199</sup> It was hoped that ene adducts (with enophiles such as PTAD and MTAD) would be compatible with synthetic base fluids and thus overcome this disadvantage. The development of synthetic lubricants first began in the early 1930s and was boosted after World War II by the shortage of petroleum base stocks.<sup>154</sup> Examples of synthetic base stocks include alkylated aromatics, aliphatic diesters, polyolesters, polyalkeneglycols and phosphate esters as well as the more costly silicones, borate esters, perfluoroethers and polyphenylene ethers.<sup>154</sup> The demands for lubricants which can perform over ever widening temperature ranges has also been a driving force for the continuing development of synthetic formulations.

### 4.2 Polyisobutenes

#### 4.2.1 Structures of Polyisobutenes

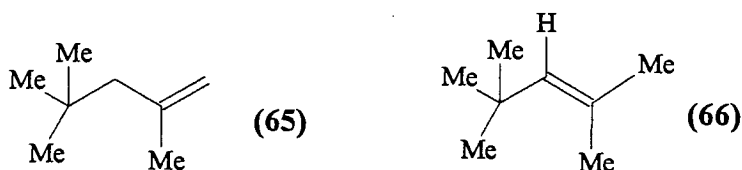
Polyisobutenes (PIBs) are synthesised by polymerisation of the C<sub>4</sub> stream from a catalytic cracking process. For this reason, the final polymer structures are complex, being formed from 1-butene, 2-butene and 2-methylbutene (isobutene) monomers. A cationic process (AlCl<sub>3</sub>/HCl or BF<sub>3</sub>/methanol) is usually employed<sup>154</sup> which favours polymerisation of isobutene. A mechanism for the formation of PIBs from isobutene is sketched in Scheme 55. Both internal and terminal double bonds are formed with the latter being favoured.



Scheme 55

#### 4.2.2 Model Studies

In order to help in the analysis of the ene addition products with PIBs, two simple compounds were chosen as models (2,4,4-trimethyl-1-pentene (65) and 2,4,4-trimethyl-2-pentene (66)) to mimic polymer Types I and II.



#### 4.2.3 Comparison of Models with Polyisobutenes

Peaks were chosen in the spectra of the model pentenes which were used to help in the assignment of spectra from four commercially obtained PIB samples (supplied by Castrol). The peaks that were chosen were from both  $^1\text{H}$



and  $^{13}\text{C}$  NMR spectra and appear in the first column Table 20, separated into the two predicted polymer structures with the double bond located in an internal or terminal position. A similar comparison has been made by other workers on a series of PIB materials (including chlorinated, hydroxy-substituted and Types I and II).<sup>200</sup> They tabulated  $^{13}\text{C}$  shift values (which confirm our assignments) but they did not describe  $^1\text{H}$  NMR analyses.

Table 20

Features of (66) (Type II structure)	NAPVIS X10	NAPVIS R	PIB 450	PIB 950
$=\text{CH}-$ 5.2ppm	Y	Y	Y	N
$=\text{C}(\text{CH}_3)_2$ 1.69, 1.73ppm	Y	Y	?	N
$=\text{CH}-$ 135ppm	Y	Y	?	N
$=\text{C}(\text{CH}_3)_2$ 19, 28ppm	?	?	?	N
Features of (65) (Type I structure)				
$=\text{CH}_2$ 4.6, 4.8ppm	Y	Y small	Y tiny	N
$=\text{C}(\text{CH}_3)\text{CH}_2-$ 1.80, 1.95ppm	Y small	N	?	N
$=\text{CH}_2$ 114ppm	Y (110ppm)	N	N	N
$=\text{C}(\text{CH}_3)\text{CH}_2-$ 25, 51ppm	Y (26 ppm) N	Y (26ppm) Y (52ppm)	Y N	N

[Y = yes, detected; N = no, not detected; ? = not assigned]

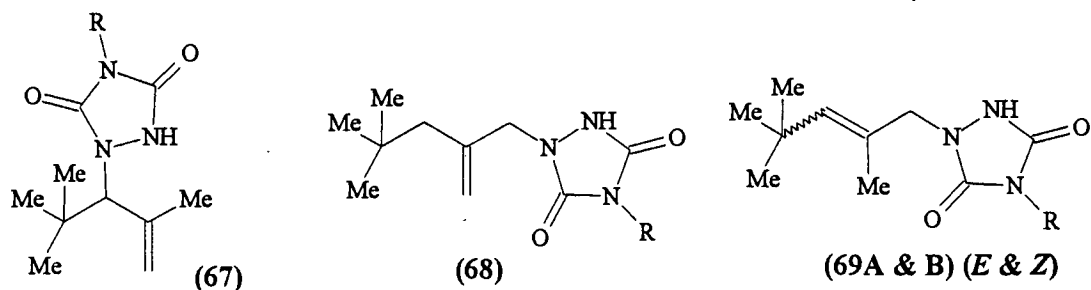
Unfortunately, the actual spectra obtained were not straightforward and did not give the simple analysis which would be predicted for polymer Types I and II, but instead contained a forest of signals in the  $^{13}\text{C}$  NMR spectra (between 12 and 38 ppm) while the  $^1\text{H}$  NMR spectra contained broad peaks in the region

0.8 - 1.8 and 1.9 - 2.1 ppm. It is thought that this complexity is probably the result of hydride and methide migrations during the polymerisation process as well as the inclusion of 1- and 2-pentene in the polymerisation feedstock. These factors would lead to the formation of less predictable polymer structures than those ideally sketched in Scheme 55. For example, in the alkene region of the PIBX proton NMR spectrum there were four groups of signals (the major group at 5.2 ppm with two smaller patterns at 4.7 and 4.85 ppm and a minor unidentified signal at 5.4 ppm). The relative intensities of the first three patterns confirms that the terminally unsaturated polymer predominates (*ie.* Type I), while the unidentified alkene signal at 5.4 ppm provides further evidence for unpredicted polymer structures (*ie.* other than Types I and II).

From analysis by mass spectroscopy the molecular masses of the polymers Napvis X10 and R were shown to be a mixture of predominantly 224 and 168 (corresponding to  $n = 4$  and 3 in Scheme 55) while PIB 450 and 950 have masses equivalent to oligomers with  $n = 6$  and 9 respectively.

#### 4.2.4 Reaction of Model Pentenes

A five-fold excess of each alkene was reacted with MTAD. The 2-pentene (66) decolourised MTAD in 80 mins while reaction of the 1-pentene (65) was much faster (only 2 mins). The excess alkenes were removed under vacuum to give near quantitative yields (98%) of the adducts. In the ene addition of these model compounds with MTAD there is one possible product (67) from the 2-pentene (66) and three (68, 69A & B) from the terminally unsaturated 1-pentene (65):



Adduct (67), derived from MTAD and the 2-pentene, was recrystallised from cyclohexane as small white crystals (mp 142-143 °C). The alkene signals were found at 4.99 and 5.01 ppm in the proton spectrum and at 117.17 and 140.11 ppm in the carbon spectrum, while the adjacent CHN signals were seen at 4.40 and 68.27 ppm in the  $^1\text{H}$  and  $^{13}\text{C}$  spectra respectively.

As expected, the 1-pentene formed a mixture of products and from the  $^1\text{H}$  NMR spectrum it was calculated that the ratio of products 68:69A:69B was 9:1:1. The major adduct (68) was selectively recrystallised from cyclohexane and melted at 119.5-120.5 °C. Its spectra contained absorptions for the alkene region at 4.96 and 5.09 ppm ( $^1\text{H}$ ) and 117.30 and 140.16 ppm ( $^{13}\text{C}$ ), while the  $\text{CH}_2\text{N}$  position appeared at 4.07 ppm and 52.43 ppm. The geometric isomers (69A) and (69B) were not separated, their alkene signals were found at 5.38 and 5.42 ppm ( $^1\text{H}$ ) and 126.51, 126.58, 141.49 and 142.00 ppm ( $^{13}\text{C}$ ) while the  $\text{CH}_2\text{N}$  signals were at 3.88 and 4.25 ppm ( $^1\text{H}$ ) and 46.60 and 55.98 ppm ( $^{13}\text{C}$ ).

A competition experiment was carried out between the two models to find out which was more reactive towards MTAD. The enophile (one equivalent) was stirred with both the alkenes (five equivalents each) in methylene chloride at room temperature. Examination of the  $^1\text{H}$  NMR spectrum revealed that the products (67, 68, 69A & 69B) were formed in the ratio 7:8:1:1. Extending these observations to the PIB compounds, structure (68) would be expected to be favoured on ene addition of MTAD.

#### 4.2.5 Modification of Polyisobutenes

Despite the complexity of the starting materials, the addition of MTAD was carried out. The PIB samples were stirred in ice-cooled dichloromethane and 1 ml aliquots of MTAD in dichloromethane were added. The time taken for the MTAD to decolourise was monitored. Napvis R was more reactive than Napvis X10 and decolourised 0.8 equivalents of MTAD, while the X10 sample was *ca.* 10 times slower and only reacted with 0.6 equivalents of the enophile. After addition to MTAD the NMR spectra of both adducts were inconclusive; they do show definite shifts from the starting alkenes but not all the expected signals can be found for the predicted adducts.

For example, the addition to PIBR resulted in absorptions in the proton NMR spectrum at 5.0 and 5.05 (possibly resulting from 68 and 67) and 4.65 and 5.2 ppm (unassigned), however no signals were visible for the predicted CHN and CH<sub>2</sub>N positions. In the corresponding <sup>13</sup>C NMR spectrum, alkene signals were found at 110, 114, 117 and 144 ppm. Those at 117 and 144 ppm could be from 68 and 67. There was no CHN signal at *ca.* 68 ppm (which might be expected for 67) although absorptions were seen at 51.7 ppm (*cf.* CH<sub>2</sub>N of 68, predicted at 52.4 ppm). FAB mass spectroscopy results confirmed the presence of adducts for varying oligomers (equivalent to *n* = 4,3,2 and 1).

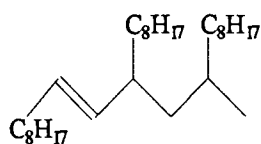
PIB450 and PIB950 were much more homogeneous by NMR than the R and X10 samples but showed little sign of unsaturation. On expansion of the alkene region of the <sup>1</sup>H NMR spectrum of PIB450, a very weak signal at *ca.* 5.2 ppm could be seen, however the corresponding <sup>13</sup>C signal could not be identified. Examination of PIB950 revealed no sign of any unsaturation. Because of the structural uncertainty of the starting materials, these high molecular weight polymers were not studied further.

## 4.3 Polyalphaolefins

### 4.3.1 Structures of Polyalphaolefins

Hydrogenated polyalphaolefins (PAOs) are fluids which are used as synthetic lubricant basestocks. They have several advantages over mineral oil basestocks: good low temperature properties, high viscosity index (*ie.* their viscosities have low variations with temperature), low volatility, high flash point, they contain no sulfur and present no toxicological problems.<sup>154</sup> However they also have some less beneficial properties: they have a low solvency to additives and are not particularly thermally stable.

PAOs are oligomers of 1-alkenes, usually 1-decene. Several polymerisation methods have been investigated<sup>154,201,202</sup> involving free-radical, Ziegler and Friedel Crafts catalysis, as well as the use of varying alkene chain lengths. Free-radical catalysis provides the least control over the degree of polymerisation and gives poor product yields. It also causes a high degree of skeletal isomerisation which can lead to undesirable and unpredictable product viscosities. Ziegler-type catalysts are capable of producing high quality oligomers in high yields although the catalysts require careful handling and are difficult to reclaim after reaction. Friedel-Crafts catalysis, using  $\text{BF}_3$  and a co-catalyst such as n-propanol or n-butanol, is the favoured method for PAO production. A typical trimer from this process is shown below (70). By controlling the reaction temperature, oligomer distribution can be controlled while the choice of co-catalyst also influences the reaction products.



(70)

The aim of this work was to modify unhydrogenated PAOs in order to synthesise friction reducing lubricant additives which might be more compatible with synthetic base fluids.

#### 4.3.2 Modification of Polyalphaolefins

A sample was supplied by Castrol which had been prepared by cationic oligomerisation. It had been separated into fractions by molecular distillation and the trimer-rich portion ( $C_{30}:C_{40} \geq 8:2$ ) was chosen for study.

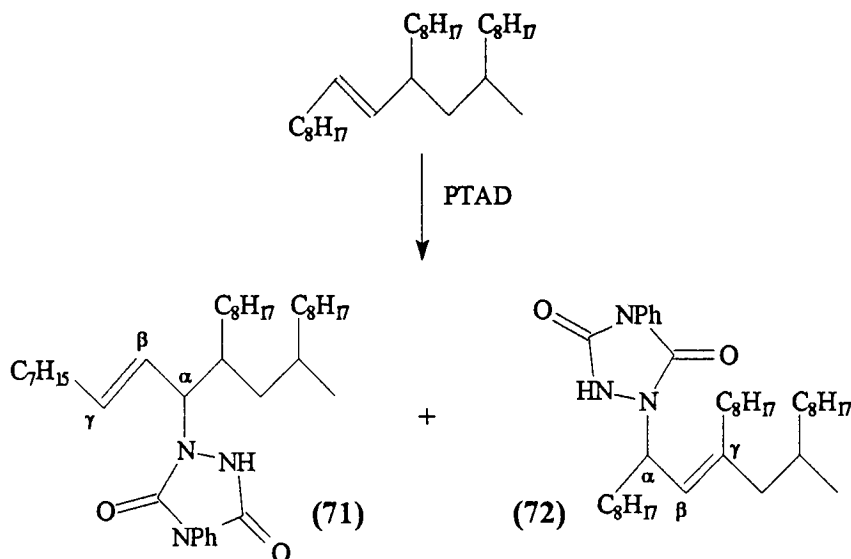
##### 4.3.2.1 Examination of Starting Materials

The starting PAO was examined by  $^1H$  and  $^{13}C$  NMR, FTIR and FAB mass spectroscopy. Expansion of the region around 5 ppm showed unsaturated proton signals whose ratio to the methyl protons was 13:147 which, coupled with the presence of several quaternary unsaturated carbon signals in the  $^{13}C$  NMR, further indicates that skeletal rearrangements are likely to have occurred during the oligomerisation process. The resultant fluid does not have the predicted ideal structure (70). The ratio of double bonds to methyl groups was estimated by NMR as *ca.* 1:8, which is half that for the predicted unisomerised material. The infra-red spectrum contains a weak C=C absorption at  $1662\text{ cm}^{-1}$  and mass spectroscopy confirms that the trimer was the major component ( $C_{30}H_{60}$ ) while some tetramer ( $C_{40}H_{80}$ ) was also present.

##### 4.3.2.2 Addition of Azo Enophiles

Two of the azo-type enophiles, PTAD and MTAD were reacted with PAO. Equimolar quantities of PTAD and PAO (based on a molecular formula of  $C_{30}H_{60} = 420$ ) were stirred in dichloromethane at  $0^\circ\text{C}$  for two hours. The reaction was slow and no colour fading was detected and so the reaction was allowed to continue overnight at room temperature to yield a milky, pale orange viscous liquid. Dry flash chromatography was used to remove

orange viscous liquid. Dry flash chromatography was used to remove unreacted starting materials. A product fraction which eluted with 60% ether in hexane was collected in 42% yield and examined by  $^1\text{H}$  and  $^{13}\text{C}$  NMR, FTIR and FAB mass spectroscopy. Scheme 56 illustrates predicted ene adduct structures for this addition.



Scheme 56

The proton NMR spectrum revealed weak absorptions between 4.4 and 5.7 ppm which, on expansion, were tentatively assigned as  $\alpha$ -CHN (the CH attached to PTAD, 4.6 ppm, m), unreacted PAO alkene (5.1 ppm, m,  $J$  10 Hz) and the new ene adduct double bond (5.4 ppm, m, H- $\beta$  and H- $\gamma$ ). Accurate mass measurements by FAB mass spectroscopy confirmed that products consistent with both the trimer/PTAD adduct and tetramer/PTAD adducts were present  $\{m/z$  (FAB) 596.51547 [ $\text{M}^+ + 1$ ,  $\text{C}_{38}\text{H}_{66}\text{N}_3\text{O}_2$  (trimer) requires 596.51547], 736.671972 [ $\text{M}^+ + 1$ ,  $\text{C}_{48}\text{H}_{86}\text{N}_3\text{O}_2$  (tetramer) requires 736.67197]}. However, in the  $^{13}\text{C}$  spectrum, the alkene region was partially masked by strong phenyl absorptions, although an alkene signal at 126 ppm was visible and was assigned to the ene adduct. The expected  $\alpha$ -CHN signal, which would be expected at *ca.* 58 ppm, was not observed.

The reaction with MTAD was more rapid, with the PAO in two molar excess over the enophile. After 35 minutes stirring at 0°C, the enophile had faded noticeably to pale pink/orange and to pale yellow after 100 minutes. The mixture was allowed to warm to room temperature and stirred overnight before being submitted to dry flash chromatography. A fraction was eluted (96% w.r.t MTAD) which was examined by  $^1\text{H}$  and  $^{13}\text{C}$  NMR and FAB mass spectroscopy. The weak signal at 57.9 ppm was attributed to  $\alpha$ -CHN while those in the alkene region were not distinct enough from baseline noise to be assigned. The proton spectrum, however, contained a multiplet at 4.5 ppm providing more evidence for the presence of the  $\alpha$ -CHN signal as well as multiple signals in the alkene region (at 4.9 - 5.2 and 5.4 ppm) which were distinct from those found in the starting PAO.

#### 4.4 Conclusion

The difficulties in analysing the reaction products from these synthetic fluids compared with the level of detail obtained in the earlier model studies and with jojoba additions results largely from uncertainties in the structures of the starting materials. Although anomalies exist between  $^1\text{H}$  and  $^{13}\text{C}$  NMR, IR and mass spectroscopy, overall the indications are that ene additions did occur although the final products could not be fully characterised.



## 5. EXPERIMENTAL

### 5.1 General

#### 5.1.1 Glossary of terms, symbols and abbreviations

conc.	concentration
d	doublet
DEAD	diethyl azodicarboxylate
DEPT	distortionless enhancement by polarisation transfer
DHMJ	dihydroxymethyl jojoba
EI	electron impact
ether	diethyl ether
FAB	fast atom bombardment
FMO	frontier molecular orbital
FTIR	Fourier transform infra red
$J$	coupling constant
$k_1'$	pseudo first order rate constant
$k_2$	second order rate constant
m	multiplet
M	moles per litre
$M^+$	molecular ion
MTAD	4-methyl-1,2,4-triazoline-3,5-dione
mmHg	pressure in mm of mercury
mol	mole
ms	mass spectroscopy
$m/z$	mass to charge ratio
NOE	nuclear Overhauser effect
PTAD	4-phenyl-1,2,4-triazoline-3,5-dione
s	singlet
t	triplet
TosNSO	<i>N</i> -Sulfinyl- <i>p</i> -toluenesulfonamide
TMS	tetramethylsilane
q	quartet
w.r.t	with respect to
$\delta$	chemical shift in ppm
$\nu_{\max}$	wavenumber of absorbance maximum

## **5.1.2 Instrumentation**

### **5.1.2.1 Centrifuge**

A Denley BR401 refrigerated centrifuge operating at 15 000 rpm was used.

### **5.1.2.2 Elemental analysis**

Elemental analyses were performed by Lorna Eades using a Perkin Elmer 2400 elemental analyser.

### **5.1.2.3 Fatty acid methyl ester (FAME) analysis**

FAME analyses were carried out by Castrol International, Analytical Services on a Hewlett Packard 5880 gas chromatograph using a chrompack 50 m x 0.25 mm Sil 88 fused silica capillary column.

### **5.1.2.4 Infra-red spectroscopy**

IR spectra were recorded as thin films, unless otherwise stated, on an SPC 3200 BIO RAD spectrophotometer (FTS-7).

### **5.1.2.5 Mass spectrometry**

Nominal and exact mass measurements under FAB ms, were recorded by Alan Taylor on a Kratos MS50TC instrument. EI ms was carried out by Elizabeth Stevenson using a Kratos MS902 spectrometer.

### **5.1.2.6 Melting points**

Melting points were measured on a Gallencamp capillary tube apparatus. A Kofler hot-stage apparatus was also used.

### **5.1.2.7 Nuclear magnetic resonance spectroscopy**

$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on Bruker WP80SY, WP200SY, AC250, WH360 and Varian VXR600 instruments by Heather Grant, John

Millar, Dr David Reed, Dr John Parkinson and Dr Ian Sadler. Two dimensional and NOE spectra were recorded on the WH360 and VXR600 machines. Chemical shifts are measured in parts per million using TMS ( $\delta = 0.0$ ) as a reference signal and coupling constants ( $J$ ) are all quoted in Hertz. Unless stated the solvent was deuterated chloroform ( $\text{CDCl}_3$ ).

#### 5.1.2.8 UV/visible spectroscopy

Monitoring of  $\lambda_{\text{max}}$  in the visible region *versus* time was carried out on a Shimadzu UV160 spectrophotometer.

### 5.1.3 Chromatography

#### 5.1.3.1 Capillary Gas Chromatography

Separation and quantitative measurement of methyl oleate and methyl elaidate was achieved on a Hewlett Packard 5880 gas chromatograph using a chrompack 50 m x 0.25 mm Sil 88 fused silica capillary column at Castrol International Technology Centre, Pangbourne, Reading with the help of Enzo Costa.

#### 5.1.3.2 Dry-flash chromatography

Dry flash column chromatography was performed using sinters with different diameters filled with Kieselgel GF<sub>254</sub> silica and eluted under a vacuum supplied by a water pump. The eluting solvents used were mixtures of the following: hexane, ether, ethyl acetate, ethanol and methanol. The compound mixture was either loaded onto the column as a solution in the initial eluting solvent or was preadsorbed onto silica.

#### 5.1.3.3 Thin layer chromatography

Preparative TLC was carried out on glass plates (20 cm x 20 cm) coated with a layer (0.5 cm) of Kieselgel GF<sub>254</sub> silica, containing 13% calcium sulphate and

a fluorescent indicator. Analytical TLC was carried out on Merck aluminium-backed plates coated with Kieselgel GF<sub>254</sub> silica (0.2 mm). Detection was achieved by UV irradiation (254 nm) and KMnO<sub>4</sub> spray (1 M, aq.). Solutions of phosphomolybdic acid and 2',7'-dichlorofluorescein in ethanol (Sigma) were also used for lipid detection.

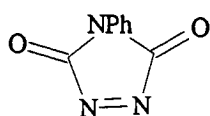
#### **5.1.4 Solvents and reagents**

All reagents were standard laboratory grade and were used as supplied unless specifically stated in the text. Solvents for general use were standard lab grade and used as supplied. Dry dichloromethane was freshly distilled from calcium hydride and then stored over molecular sieve. Toluene was dried with sodium wire.

## 5.2 Synthesis of Enophiles

### 5.2.1 4-Phenyl-1,2,4-triazolinedione (PTAD) (73)

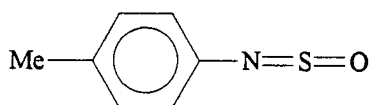
To an ice-cooled solution of 4-phenylurazole (3.54 g, 20 mmol) in dichloromethane (200 ml) was added *N*-bromosuccinimide (7.13 g, 40 mmol) and the mixture stirred for 15 min. The red solution was washed three times with water, dried ( $\text{MgSO}_4$ ) and the solvent evaporated. The crude product was sublimed in a cold finger apparatus (0.015 mbar, 80-100°C) to yield a carmine red crystalline solid (2.61 g, 74%), sublimed at 168-169°C (lit.<sup>203</sup> sublimed at 169°C)



(73)

### 5.2.2 *N*-Sulfinyl-*p*-toluenesulfonamide (TosNSO) (74)

A mixture of *p*-toluenesulfonamide (5.0 g, 0.064 mol) and freshly distilled thionyl chloride (10.0 ml, 0.14 mol) were heated to maintain a gentle reflux (oil bath temperature 80-90°C) for 8.5 h. After cooling to room temperature no solid precipitated from the golden yellow liquid. The excess thionyl chloride was removed under vacuum and trapped in a cardice/acetone bath. The resulting orange oil was submitted to Kugelröhr distillation (125°C, 0.02 mbar). The middle fraction was collected as a yellow oil, which crystallised on standing to a bright yellow solid (3.67 g, 0.017 mol, 26%), m.p. 47-51°C (lit.<sup>167</sup> m.p. 53°C)



(74)

### 5.3 Preparation of *trans*-Jojoba

2M aqueous sodium nitrite was added to a solution of jojoba (10 g, 16.2 mmol) in hexane (10 ml) and the mixture heated to reflux. 6M HNO<sub>3</sub> (0.33 ml, 2.0 mmol) was added, by drops, over 5 min and refluxed for 20 min. The mixture was immediately transferred to a separating funnel and washed with hot water (5x 10 ml at 50°C), until pH 7 was reached. The solvent was removed and residual water was removed under high vacuum. The product was a white solid (m.p. 35 - 37°C). The jojoba had undergone 59% *cis* to *trans* isomerisation by <sup>13</sup>C NMR-estimation of the *cis* and *trans* allylic signals at 27.1 and 32.5 ppm respectively. To enrich the ratio of *trans*:*cis*-jojoba, a portion was dissolved in hexane and centrifuged at 20°C, 15 000 revs<sup>-1</sup> for 20 min. The jojoba solution in hexane was decanted leaving a white solid which contained 96% *trans*-jojoba (0.1 g, 0.16 mmol).

### 5.4 Reactions of PTAD

#### 5.4.1 General procedure

The ene component (one equivalent unless otherwise stated) was magnetically stirred in dichloromethane at 0°C and the crystalline PTAD was added in one portion. Stirring was continued until the bright red colour of the PTAD had faded to colourless; the reaction was also monitored by TLC. If the unreacted ene component was volatile then it was removed under vacuum with the dichloromethane, otherwise the crude reaction mixture was submitted to dry-flash chromatography (silica, gradient hexane/ether) to recover any unreacted alkene, followed by the ene-adduct(s) in increasing polarity.

Each of the following section headings refers to the alkene being reacted with PTAD.

#### 5.4.2 *cis*-3-Hexene

*cis*-3-Hexene (0.211 g, 2.2 mmol) and PTAD (0.437 g, 2.5 mmol) were reacted as in the general procedure. After removal of the solvent and residual unreacted hexene the product was recrystallised (cyclohexane) to yield 1-(2-hexen-4-yl)-4-phenyl-1,2,4-triazoline-3,5-dione (**10**) as a white solid (0.533 g, 89%), m.p. 102-103°C, (Found: C, 64.35; H, 6.42; N, 15.93.  $C_{14}H_{17}N_3O_2$  requires C, 64.85; H, 6.61; N, 16.20%);  $\delta_H$  (200 MHz) 0.87 (3H, t,  $J$  7.3, 6-H), 1.64 (3H, dd,  $J$  7.0 and 0.7, 1-H), 1.69 (2H, m, 5-H), 4.47 (1H, q,  $J$  7.6, 4-H), 5.42 (1H, ddq,  $J$  15.4, 7.4 and 1.6, 3-H), 5.74 (1H, dqd,  $J$  15.3, 6.4 and 0.8, 2-H), 7.29-7.53 (5H, m, Ph), 9.65 (1H, br s, NH);  $\delta_C$  (50 MHz) 10.41 (C-6), 17.52 (C-1), 24.96 (C-5), 59.87 (C-4), 125.31, 127.82, 128.74, 131.10 (Ph), 126.74, 130.40 (C-2, C-3), 152.05, 153.61 (C=O).

#### 5.4.3 *trans*-3-Hexene

*trans*-3-Hexene (0.211 g, 2.2 mmol) and PTAD (0.437 g, 2.5 mmol) were reacted as in the general procedure. After removal of the solvent and residual unreacted hexene the product was recrystallised (cyclohexane) to yield 1-(2-hexen-4-yl)-4-phenyl-1,2,4-triazoline-3,5-dione (**10**) as a white solid (0.447 g, 75%) identical to that from *cis*-3-hexene,  $\delta_H$  (200 MHz) 0.90 (3H, t,  $J$  7.3, 6-H), 1.66 (3H, dm,  $J$  6.5, 1-H), 1.69 (2H, m, 5-H), 4.49 (1H, q,  $J$  7.5, 4-H), 5.44 (1H, ddq,  $J$  15.4, 7.2 and 1.5, 3-H), 5.76 (1H, dqd,  $J$  15.4, 6.4 and 0.9, 2-H), 7.31-7.55 (5H, m, Ph), 10.51 (1H, br s, NH);  $\delta_C$  (50 MHz) 10.52 (C-6), 17.64 (C-1), 25.05 (C-5), 59.92 (C-4), 125.37, 126.79, 128.86, 131.18 (Ph), 127.93, 130.59 (C-2, C-3), 152.15, 153.85 (C=O).

#### 5.4.4 *trans*-5-Decene

*trans*-5-Decene (0.422 g, 3.0 mmol) and PTAD (0.437 g, 2.5 mmol) were reacted as in the general procedure. After removal of the solvent and residual unreacted decene the product was recrystallised (cyclohexane) to yield 1-(4-

decen-6-yl)-4-phenyl-1,2,4-triazoline-3,5-dione (9) as a white solid (0.761 g, 80%), m.p. 70.7-72.0°C. (Found: C, 68.79; H, 8.09; N, 13.43.  $C_{18}H_{25}N_3O_2$  requires C, 68.54; H, 7.99; N, 13.32%);  $\delta_H$  (200 MHz) 0.80-0.92 (6H, m, 1-H and 10-H), 1.20-1.44 (6H, m, 2-H, 8-H and 9-H), 1.66 (2H, m, 7-H) [diastereotopic at 360 MHz], 1.97 (2H, q,  $J$  6.9, 3-H), 4.58 (1H, q,  $J$  7.4, 6-H), 5.43 (1H, ddt,  $J$  15.4, 7.4 and 1.3, 5-H), 5.75 (1H, dtd,  $J$  15.4, 7.0 and 0.5, 4-H), 7.31-7.53 (5H, m, Ph), 9.55 (br s, NH);  $\delta_C$  (50 MHz) 13.41, 13.75 (C-1 and C-10), 21.82, 22.05 (C-8 and C-9), 28.01 (C-2), 31.54 (C-7), 34.16 (C-3), 58.50 (C-6), 125.30, 127.88, 128.81, 131.21 (*o*, *p*, *m* and *i*-Ph), 125.88 (C-5), 135.58 (C-4), 152.16, 153.98 (C=O).

#### 5.4.5 *cis*-5-decene

*cis*-5-Decene (0.078 g, 0.6 mmol) and PTAD (0.087 g, 0.5 mmol) were reacted as in the general procedure. After removal of the solvent and residual unreacted decene the product was recrystallised (cyclohexane) to yield 1-(4-decen-6-yl)-4-phenyl-1,2,4-triazoline-3,5-dione (9) as a white solid (0.102 g, 65%), m.p. 70.7-71.6°C. (Found: C, 68.02; H, 8.00; N, 13.36.  $C_{18}H_{25}N_3O_2$  requires C, 68.54; H, 7.99; N, 13.32%);  $\delta_C$  (63 MHz) 13.42, 13.76 (C-1 and C-10), 21.84, 22.07 (C-8 and C-9), 28.04 (C-2), 31.54 (C-7), 34.18 (C-3), 58.50 (C-6), 125.29, 127.89, 128.83, 131.21 (*o*, *p*, *m* and *i*-Ph), 125.88 (C-5), 135.62 (C-4), 152.16, 153.98 (C=O).

#### 5.4.6 Methyl oleate

Methyl oleate (1.48 g, 5.0 mmol) and PTAD (0.82 g, 4.7 mmol) were reacted as in the general procedure. After 40 min the mixture was colourless. The solvent was removed and the mixture submitted to dry flash chromatography to yield in increasing polarity:

- (i) recovered methyl oleate (0.125 g, 8%)



- (ii) monoadducts (**13 A&B**) (2.16 g, 92%) as an orange oil which solidified to a pale orange solid *1-(8-[10]-octadecen-10[8]-oyl)-4-phenyl-1,2,4-triazoline-3,5-dione*,  $\nu_{\text{max}}/\text{cm}^{-1}$  3166, 3057 (N-H), 1695 (C=O), 1503 (N-H bend) and 968 (*trans* C=C). For  $^1\text{H}$  and  $^{13}\text{C}$  assignments see Appendix 1.

#### 5.4.7 Methyl elaidate

Methyl elaidate (1.49 g, 5.0 mmol) and PTAD (0.87 g, 4.7 mmol) were reacted as in the general procedure. After 150 min the mixture was colourless. The solvent was removed and the mixture submitted to dry flash chromatography to yield in increasing polarity:

- (i) recovered methyl elaidate (0.061 g, 4%)
- (ii) monoadducts (**13A&B**) (2.21 g, 94%) as an orange oil which solidified to a pale orange solid *1-(8-[10]-octadecen-10[8]-oyl)-4-phenyl-1,2,4-triazoline-3,5-dione*,  $\nu_{\text{max}}/\text{cm}^{-1}$  3166, 3057 (N-H), 1682 (C=O), 1503 (N-H bend) and 967 (*trans* C=C). For  $^1\text{H}$  and  $^{13}\text{C}$  assignments see Appendix 2.

#### 5.4.8 Oleyl Acetate

Oleyl acetate (0.953 g, 3.1 mmol) and PTAD (0.56 g, 3.2 mmol) were reacted as in the general procedure. After 90 min the mixture was colourless. The solvent was removed and the mixture submitted to dry flash chromatography to yield in increasing polarity:

- (i) recovered oleyl acetate (0.015 g, 2%)
- (ii) monoadducts (**14A&B**) (1.323 g, 93%). For  $^1\text{H}$  and  $^{13}\text{C}$  assignments see Appendix 3.

### 5.4.9 Jojoba oil

Two ratios of jojoba:PTAD were reacted together as in the general procedure and purified by dry flash chromatography to give the product distributions shown in Table 21.

Table 21

Reactant Ratios			Product Yields		
	jojoba	PTAD	recovered jojoba	monoadducts (15)	diadducts (16)
(i)	3.59 g 5.8 mmol	1.00 g 5.7 mmol	41%	37%	16%
(ii)	1.76 g 2.9 mmol	1.00 g 5.7 mmol	18%	24%	58%

$m/z$  (FAB) 792.66185 [ $M^+ + 1$ ,  $C_{50}H_{86}N_3O_4$  ( $m+n=21$ , 1:1 adduct) (15) requires 792.66179],  $m/z$  (FAB) 967.70002 [ $M^+ + 1$ ,  $C_{58}H_{90}N_6O_6$  ( $m+n=21$ , 2:1 adduct) (16) requires 967.69997];  $\nu_{\max}/\text{cm}^{-1}$  3175, 3076 (NH), 1695 (C=O), 1503 (NH bend) and 971 (C=C). For  $^1\text{H}$  and  $^{13}\text{C}$  assignments see Appendices 4&5.

### 5.4.10 *Trans*-Jojoba

*Trans*-jojoba (0.054 g, 0.09 mmol) and PTAD (0.024 g, 0.14 mmol) were reacted together as in the general procedure. After solvent removal, the residue was submitted to preparative TLC and a pure sample of the monoadducts was obtained. This was examined by  $^1\text{H}$  NMR (360 MHz) and found to be identical to (15) apart from in the residual unsaturated signals, H-11 and H-12. Selected  $^1\text{H}$  absorptions are shown below (Table 22) for comparison with Appendix 5

Table 22

H	$\alpha$	$\beta$	$\gamma$	$\delta$	$\epsilon$	11,12	10,13
$\delta/\text{ppm}$	4.58	5.44	5.77	2.02	ca. 1.7	5.37	1.95
m	q	dd	dt	q		t	m
$J/\text{Hz}$	7.4	15.5, 7.1	15.4, 6.8	6.9		3.6	

### 5.4.11 1,4-Pentadiene

1,4-Pentadiene (0.31 ml, 0.20 g, 3.0 mmol) was stirred with PTAD (0.175 g, 1.0 mmol) as in the general procedure. After 2h the solution was still pale pink in colour and was allowed to stir overnight at room temperature. The solvent and unreacted pentadiene were removed under vacuum to furnish a 2:1 adduct of PTAD:the diene as a white solid (**54**) (0.195 g, 93%). The solid was polar ( $R_f = 0.4$  in ethyl acetate) and did not recrystallise successfully.  $m/z$  (FAB) 419.14676 ( $M^+ + 1$ ,  $C_{21}H_{19}N_6O_4$  requires 419.14677).  $^{13}C$  NMR on the crude solid showed the compound to be pure.  $\delta_C$  (50 MHz) 44.35, 46.88 (C-5' and C-8), 50.89 (C-5), 122.06, 123.29 (C-6 and C-7), 125.80, 125.92, 128.30, 128.98, 130.62, 130.85 (Ph), 151.59, 152.75, 153.48, 153.68 (C=O). For  $^1H$  NMR assignments see Table 14.

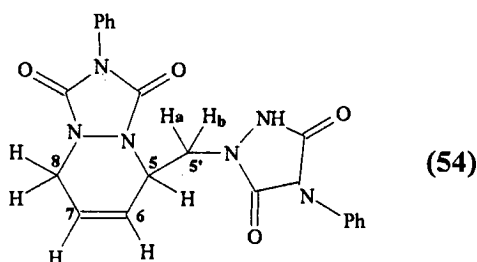


Table 14

H	$\delta_H$ /ppm (360 MHz)	$J_{x,y}$ /Hz
5'a	3.97 <sup>a</sup>	5'a,5
5'b	3.60, dd	5'b,5'a
		5'b,5
5	4.83, m	5,6
		5,7
6	5.69, dm	6,7
		6,8a
		6,8b
7	5.92, dt	7,8a
		7,8b
8a	4.24, ddd	8a,8b
8b	3.95 <sup>a</sup>	
Ph	7.23-7.47, m	
NH	8.95, br s	

a: 5'a and 8b overlap

#### 5.4.12 *cis-2-trans-4-hexadiene*

*cis-2-trans-4-hexadiene* (0.25 ml, 0.18 g, 2.2 mmol) was stirred with PTAD (0.384 g, 2.2 mmol) as in the general procedure. The bright red colour disappeared within 90 s to give one product by TLC (**56**) (0.54 g, 96%), m.p. 167.5-169°C (from ethanol) (lit.<sup>194</sup> 169.5-170.5°C). (Found: C, 65.27; H, 5.95; N, 16.38. C<sub>14</sub>H<sub>15</sub>N<sub>3</sub>O<sub>2</sub> requires C, 65.36; H, 5.88; N, 16.33%). For <sup>1</sup>H NMR assignments see Table 23. δ<sub>C</sub> (50 MHz) 16.37 (C-6'), 49.81 (C-6), 124.99 (C-7), 125.76, 127.69, 128.80, 131.04 (Ph), 152.14 (C=O)

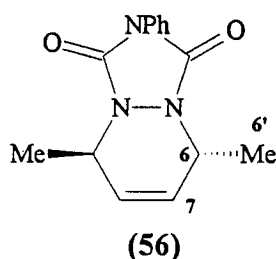


Table 23

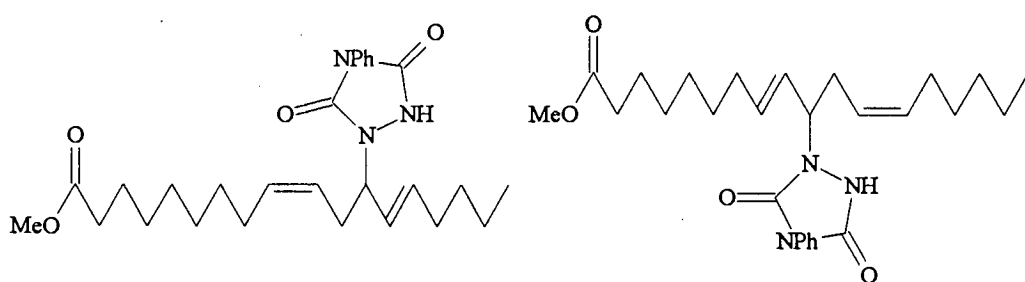
H	δ <sub>H</sub> /ppm (200 MHz)	<i>J</i> <sub>x,y</sub> /Hz	
6'	1.30, d	6',6	6.5
6	4.54, dq	6,6'	6.5
		6,7	2.5
7	5.81, d	7,6	2.5
Ph	7.25-7.56, m	-	-

#### 5.4.13 Methyl linoleate

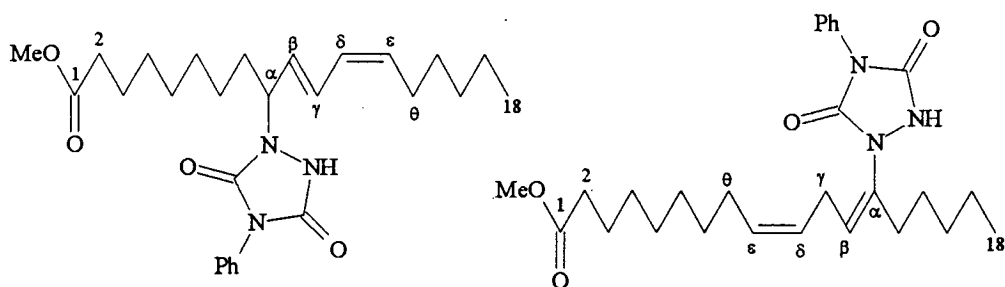
Methyl linoleate (0.73 g, 2.5 mmol) was stirred with PTAD (0.437 g, 2.5 mmol) as in the general procedure. The colour faded rapidly within the first 60 s and was pale orange after 2.5 min. The crude material was submitted to dry-flash chromatography (silica, hexane/ether/ethyl acetate and methanol) to give, in order of elution:

- (i) recovered methyl linoleate (32%) identified by comparison with an authentic sample by TLC and <sup>1</sup>H NMR

- (ii) 1:1 ene adducts (46 & 47) (36%) as an oil 1-(8-E[10-E], 12-Z[9-Z]-octadecen-10[12]-oyl)-4-phenyl-1,2,4-triazoline-3,5-dione *m/z* (FAB) 470.30189 ( $M^+ + 1$ ,  $C_{27}H_{40}N_3O_4$  requires 470.30186), for  $^1H$  and  $^{13}C$  assignments see Appendix 6. Although this is the major product, traces *ca.* 9% of the alternative ene-adducts, where the double bonds are shifted into conjugation 48 & 49) can be seen in the  $^1H$  NMR (Table 24). Weaker intensity signals in the  $^{13}C$  NMR further confirm the presence of compounds (48 & 49).



(46 & 47))



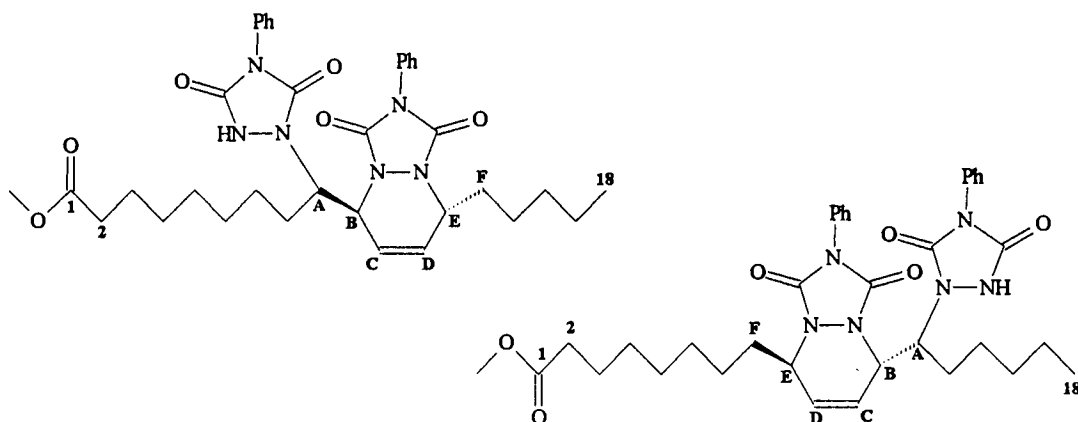
(48 & 49)

Table 24

Selected  $^1H$  NMR data for traces of  
compounds 48 & 49

H	$\delta_H/ppm, m$	$J_{x,y}/Hz$
$\beta$	5.58, dd	$\beta\gamma$ 15, $\beta\alpha$ 8
$\gamma$	6.52, dd	$\gamma\beta$ 15, $\gamma\delta$ 11
$\delta$	5.87, t	$\delta\epsilon$ and $\delta\gamma$ 10.5

- (iii) 2:1 tandem ene/Diels-Alder adducts (**50 & 51**) (32%) as a mixture of diastereomers in a 5:6 ratio;  $m/z$  (FAB) 645.34010 ( $M^+ + 1$ ,  $C_{35}H_{45}N_6O_6$  requires 645.34003), for  $^1H$  and  $^{13}C$  assignments see Appendix 7.



(**50 & 51**)

#### 5.4.14 Polyalphaolefin (PAO)

PAO (trimer,  $C_{30}H_{60}$ ) (2.12 g, 5 mmol) and PTAD (0.873 g, 5 mmol) were reacted as in the general procedure. The reaction was slow; after 90 min there was no appreciable colour fading in the PTAD colour. The mixture was allowed to warm to room temperature and stirred overnight to give a viscous milky-orange liquid. Predictably, TLC of the product showed broad streaking as the PAO itself is a mixture of  $C_{30}$  and  $C_{40}$  oligomers. The mixture was submitted to dry flash chromatography and after removal of unreacted PAO (17%) a cut of the product fraction was collected (42%). This was examined by  $^1H$  and  $^{13}C$  NMR and FAB ms. Phenyl signals were evident in the NMR spectra as well as weak  $C=O$  peaks. However, the expected  $CHN$  signals at *ca.*  $\delta_H$  4.5 ppm and  $\delta_C$  58.5 ppm were not detected. Evidence for the adduct formation was seen in the ms;  $m/z$  (FAB) 596.51547 [ $M^+ + 1$ ,  $C_{38}H_{66}N_3O_2$  (trimer) requires 596.51547], 736.671972 [ $M^+ + 1$ ,  $C_{48}H_{86}N_3O_2$  (tetramer) requires 736.67197]

## 5.5 Reactions of DEAD

### 5.5.1 General Procedure

The ene component (one equivalent, unless otherwise stated) was dissolved in 1,1,1-trichloroethane and the liquid DEAD (one equivalent) was added in one portion. The solution was heated under reflux until the bright orange colour of the DEAD had faded; the reaction was also monitored by TLC. If the unreacted ene component was volatile then it was removed under vacuum with the solvent. Otherwise the crude reaction mixture was submitted to dry flash chromatography (silica, gradient hexane/ether) to recover any unreacted alkene, followed by the ene adduct(s) in increasing polarity. In the case of the lower boiling 1-alkenes (1-hexene, 1-octene and 1-decene) a small-scale cold-finger distillation apparatus was used to purify the products, instead of chromatography.

### 5.5.2 1-Alkene series

The 1-alkenes listed below were refluxed (in 1,2-dichloroethane) at 75-80°C as in the general procedure to give the following adducts. For  $^1\text{H}$  and  $^{13}\text{C}$  NMR data on these compounds (a-h) see Appendix 8. Small amounts of diadduct formation (where a second mole of DEAD reacted with the 1:1 ene adduct) was evident in the mass spectrum, but this is not quantified. Appendix 8 also gives an estimate of the amounts of *cis*-isomer present (from  $^{13}\text{C}$  NMR intensity comparisons).

(a) 1-hexene (21.00 g, 250 mmol) was refluxed with DEAD (8.71 g, 50 mmol) for 20 h. After removal of the excess alkene and solvent, distillation yielded 1,2-hydrazinedicarboxylic acid, 1-(2-hexenyl)-diethyl ester (*E*) (**75**) (9.80 g, 76%),  $m/z$  (FAB) 259.16579 ( $\text{M}^+ + 1$ ,  $\text{C}_{12}\text{H}_{23}\text{N}_2\text{O}_4$  requires 259.16577), 433.22982 [ $\text{M}^+ + 1$  (2:1 adduct),  $\text{C}_{18}\text{H}_{33}\text{N}_4\text{O}_8$  requires 433.22981].

(b) 1-octene (14.0 g, 125 mmol) was refluxed with DEAD (4.35 g, 25 mmol) for 14 h. After removal of the excess alkene and solvent, distillation yielded 1,2-hydrazinedicarboxylic acid, 1-(2-octenyl)-diethyl ester (*E*) (**76**) (4.79 g, 67%),  $m/z$  (FAB) 287.197074 ( $M^+ + 1$ ,  $C_{14}H_{27}N_2O_4$  requires 287.19707), 461.26114 [ $M^+ + 1$  (2:1 adduct),  $C_{20}H_{37}N_4O_8$  requires 461.26112].

(c) 1-decene (17.55 g, 125 mmol) was refluxed with DEAD (4.37 g, 25 mmol) for 8 h. After removal of the excess alkene and solvent, distillation yielded 1,2-hydrazinedicarboxylic acid, 1-(2-decenyl)-diethyl ester (*E*) (**77**) (6.52 g, 83%),  $m/z$  (FAB) 315.22836 ( $M^+ + 1$ ,  $C_{16}H_{31}N_2O_4$  requires 315.22837), 489.29243 [ $M^+ + 1$  (2:1 adduct),  $C_{22}H_{41}N_4O_8$  requires 489.29242].

(d) 1-dodecene (26.63 g, 125 mmol) was refluxed with DEAD (4.37 g, 25 mmol) for 7.5 h. Dry flash chromatography was used to remove the excess alkene followed by distillation to yield 1,2-hydrazinedicarboxylic acid, 1-(2-dodecenyl)-diethyl ester (*E*) (**78**) (5.73 g, 67%),  $m/z$  (FAB) 343.25965 ( $M^+ + 1$ ,  $C_{18}H_{35}N_2O_4$  requires 343.25966), 517.32368 [ $M^+ + 1$  (2:1 adduct),  $C_{24}H_{45}N_4O_8$  requires 517.32371].

(e) 1-tetradecene (21.95 g, 112 mmol) was refluxed with DEAD (3.89 g, 22 mmol) for 9.25 h. Dry flash chromatography was used to remove the excess alkene followed by distillation to yield 1,2-hydrazinedicarboxylic acid, 1-(2-tetradecenyl)-diethyl ester (*E*) (**79**) (6.02 g, 73%),  $m/z$  (FAB) 371.290961 ( $M^+ + 1$ ,  $C_{20}H_{39}N_2O_4$  requires 371.29096), 545.35501 [ $M^+ + 1$  (2:1 adduct),  $C_{26}H_{49}N_4O_8$  requires 545.35499].

(f) 1-hexadecene (28.03 g, 125 mmol) was refluxed with DEAD (4.37 g, 25 mmol) for 13.5 h. Dry flash chromatography was used to remove the excess alkene followed by distillation to yield 1,2-hydrazinedicarboxylic acid, 1-(2-hexadecenyl)-diethyl ester (*E*) (**80**) (6.67 g, 67%),  $m/z$  (FAB) 399.32227



( $M^+ + 1$ ,  $C_{24}H_{43}N_2O_4$  requires 399.32226), 573.39629 [ $M^+ + 1$  (2:1 adduct),  $C_{28}H_{53}N_4O_8$  requires 573.38631].

(g) 1-octadecene (19.77 g, 78 mmol) was refluxed with DEAD (2.71 g, 15.6 mmol) for 14.5 h. Dry flash chromatography was used to remove the excess alkene followed by distillation to yield 1,2-hydrazinedicarboxylic acid, 1-(2-octadecenyl)-diethyl ester (*E*) (81) (5.65 g, 85%),  $m/z$  (FAB) 427.35357 ( $M^+ + 1$ ,  $C_{24}H_{47}N_2O_4$  requires 427.35357), 601.41765 [ $M^+ + 1$  (2:1 adduct),  $C_{30}H_{57}N_4O_8$  requires 601.41761].

(h) 1-eicosene (17.20 g, 61 mmol) was refluxed with DEAD (2.13 g, 12 mmol) for 25 h. Dry flash chromatography was used to remove the excess alkene followed by distillation to yield 1,2-hydrazinedicarboxylic acid, 1-(2-eicosenyl)-diethyl ester (*E*) (82) (4.45 g, 80%),  $m/z$  (FAB) 455.38485 ( $M^+ + 1$ ,  $C_{26}H_{51}N_2O_4$  requires 455.38486), 629.44893 [ $M^+ + 1$  (2:1 adduct),  $C_{32}H_{60}N_4O_8$  requires 629.44891].

#### 5.5.2.1 Hydrogenation of 1-alkene/DEAD adducts

The adducts (75, 77, 79, 81) (*ca.* 2 mmol) in 10 ml ethanol were stirred with 10% Pd-C (1.7 mg) while  $H_2$  was admitted overnight from a balloon. In each case, after filtration through celite and solvent removal,  $^1H$  NMR was used to confirm that the unsaturated region  $\delta_H$  5.3-5.6 ppm had been removed. Reaction times, yields and mass spectroscopy data for each adduct are shown in Table 25. For  $^1H$  and  $^{13}C$  NMR data see Appendix 9.

Table 25

hydrogenated adduct of :	product compound number	reaction time/h	yield %	$m/z$ (FAB) found:	$M^+ + 1$ requires
hexene (75)	(83)	18	94	261.18146	261.18142
decene (77)	(84)	18.5	99	317.24401	317.24402
tetradecene (79)	(85)	25	90	373.30660	373.30661
octadecene (81)	(86)	46	98	429.36925	429.36921

### 5.5.3 *trans*-3-Hexene

*trans*-3-Hexene (0.41 g, 4.9 mmol) was refluxed at 84°C with DEAD (0.82g, 4.7 mmol) in dichloroethane for 16 h. After removal of the solvent and excess unreacted alkene, the residue (86%) was submitted to dry flash chromatography. A small quantity of DEAD was recovered (3%), followed by the 1:1 ene adduct 1,2-hydrazinedicarboxylic acid, 1-(2-hexen-4-yl)-diethyl ester (*E*) (22) (58%),  $m/z$ (FAB) 433.22986 ( $M^++1$ ,  $C_{18}H_{33}N_4O_8$  requires 433.22982),  $\delta_H$  (200 MHz) 0.83 (3H, t,  $J$  7.3,  $\omega$ -H), 1.182 and 1.189 (6H, 2xt,  $J$  7.1, DEAD  $CO_2CH_2CH_3$ ), 1.47 (2H, m,  $\epsilon$ -H), 1.61 (3H, dd,  $J$  6.2 and 0.7,  $\delta$ -H), 4.11 (4H, q,  $J$  7.0, DEAD  $CO_2CH_2CH_3$ ), 4.36 (1H, q,  $J$  7.6,  $\alpha$ -H), 5.34 (1H, ddm,  $J$  16.0, 7.5 and 1.0,  $\beta$ -H), 5.57 (1H, dq,  $J$  15.4 and 6.1,  $\gamma$ -H), 6.54 (1H, br s, NH);  $\delta_C$  (50 MHz) 10.57 (C- $\omega$ ), 14.23 (DEAD  $CO_2CH_2CH_3$ ), 17.59 (C- $\delta$ ), 24.59 (C- $\epsilon$ ), 61.56, 61.98 (DEAD  $CO_2CH_2CH_3$  and concealed C- $\alpha$  cf. Compound (23), Section 5.5.4), 128.11 (C- $\beta$ ), 128.68 (C- $\gamma$ ), 155.95 and 156.72 (C=O).

*Cis*-3-Hexene was reacted as above, after solvent removal the crude yield was 77%. Purification by dry flash chromatography again furnished (22). The  $^1H$  NMR was superimposable on that of the *trans*-3-hexene adduct. Furthermore, all  $^{13}C$  peaks attributable to the *trans*-3-hexene adduct were also seen in the *cis*-3-hexene adduct spectrum. A  $^1H$  NMR spiking experiment provided alternative evidence that both initial geometries led to the same adduct.

### 5.5.4 Methyl oleate

Methyl oleate (1.48 g, 5.0 mmol) was refluxed with DEAD (0.88 g, 5.0 mmol) in dichloroethane for 23 h. After solvent removal, the residue was submitted to dry flash chromatography to yield:

- (i) recovered methyl oleate (23%), identified by TLC and  $^1H$  NMR

- (ii) 1:1 ene adducts *1,2-hydrazinedicarboxylic acid, 1-(8[10]-octadecen-10[8]- oyl)-diethyl ester (E) (23)* (60%). For  $^1\text{H}$  and  $^{13}\text{C}$  NMR data see Appendix 10.
- (iii) a more polar compound (16%), which from NMR evidence, could be a 2:1 adduct of DEAD:methyl oleate similar to those observed in the mass spectra of the 1-alkene/DEAD adducts (Section 5.5.2 and Appendix 9).

### 5.5.5 Methyl elaidate

Methyl elaidate (1.47 g, 5.0 mmol) and DEAD (0.87 g, 5.0 mmol) were reacted as for methyl oleate (Section 5.5.4). The reaction was faster (11 h) and the product ratios, after dry flash chromatography were:

- (i) recovered methyl elaidate (18%)
- (ii) 1:1 ene adducts *1,2-hydrazinedicarboxylic acid, 1-(8[10]-octadecen-10[8]- oyl)-diethyl ester (E) (23)* (71%) whose  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were superimposable on those of the methyl oleate monoadducts.
- (iii) polar fraction (11%) similar to that from methyl oleate.

### 5.5.6 Jojoba

Jojoba (1.84 g, 3.0 mmol) and DEAD (1.04 g, 6.0 mmol) were refluxed in trichloroethane for 33 h. After solvent removal, the residue was submitted to dry flash chromatography to yield, in order of increasing polarity:

- (i) recovered jojoba (19%), identified by  $^1\text{H}$  NMR and TLC
- (ii) singly modified jojoba (**24**) (37%);  $\delta_{\text{H}}$  (200 MHz) 0.82 (6H, t,  $J$  6.3,  $\omega$ -H), 1.16-1.21 ( $\text{CH}_2$  envelope and DEAD  $\text{CH}_3$ ), 1.56 (quin,  $J$  6.7, 3-H), 1.96 (6H, m,  $\delta$ -H, 10-H and 13-H), 2.23 (2-H, t,  $J$  7.4, 2-H), 4.00 (2H, t,  $J$  6.7, A-H), 4.12 (4H, q,  $J$  7.1, DEAD  $\text{CO}_2\text{CH}_2\text{CH}_3$ ), 4.46 (1H, q,  $J$  6.8,  $\alpha$ -H), 5.29 (2H, t,  $J$  4.6, 11-H and 12-H), *ca.* 5.3 [ $\beta$ -H (partially

concealed by residual *cis*-alkene protons 11-H and 12-H)], 5.55 (1H, dt, *J* 15.4 and 6.4,  $\gamma$ -H), 6.37 (1H, NH);  $\delta_C$  (50 MHz) (C- $\omega$ ), 14.28 (DEAD CH<sub>3</sub>), 22.45 [C-19 and C-( $\omega$ -1)], 24.79 (C-3), 25.72, 25.97 (C-C), 26.98 (C-10 and C-13), 28.45 (C-B), 28.93-29.54 (CH<sub>2</sub> envelope), 31.67 [C-( $\omega$ -2)] 32.18 (C- $\delta$ ), 34.15 (C-2), 59.81 (C- $\alpha$ ), 61.62, 62.00 (DEAD CH<sub>2</sub>), 64.15 (C-A), 127.50 (C- $\gamma$ ), 129.65 (C-11 and C-12), 133.61 (C- $\beta$ ), 155.85 (DEAD C=O), 173.71 (C-1).

- (iii) doubly modified jojoba (**25**) (35%);  $\delta_H$  (200 MHz) 0.81 (6H, t, *J* 6.2,  $\omega$ -H), 1.12-1.30 (CH<sub>2</sub> envelope and DEAD CH<sub>3</sub>), 1.54 (quin, *J* 6.6, 3-H), 1.94 (4H, m,  $\delta$ -H), 2.22 (2-H, t, *J* 7.4, 2-H), 3.99 (2H, t, *J* 6.7, A-H), 4.06-4.18 (m, DEAD CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 4.44 (2H, q, *J* 7.1,  $\alpha$ -H), 5.31 (2H, dd, *J* 15.6 and 7.3,  $\beta$ -H), 5.54 (2H, dt, *J* 15.5 and 6.5,  $\gamma$ -H), 5.28 (m, trace of residual *cis*-double bonds), 6.39 and 6.81 (2x br s, NH);  $\delta_C$  (90 MHz) similar to 1:1 adduct with C- $\delta$  and DEAD signals increased in intensity; only residual traces of C-10, 11, 12 and 13, extra signals at 61.80, 62.53 and 63.75 and small absorptions at 122.90 and 137.81 ppm.

### 5.5.7 Methyl linoleate

Two ratios of methyl linoleate : DEAD were reacted together as in the general procedure and purified by dry flash chromatography to give the product distributions shown below in Table 15:

Table 15

Reactant Ratios			Reaction time	Product yields			
methyl linoleate	DEAD			recovered alkene	1:1 ene adducts (61)	tandem ene/D-A (62)	other 2:1 adducts
(i) 0.592 g 2.0 mmol	0.348 g, 2.0 mmol		48 h	13%	67%	4%	7%
(ii) 0.294 g 1.0 mmol	0.348 g 2.0 mmol		120 h	trace	38%	16%	20%

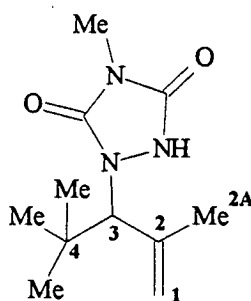
The recovered methyl linoleate was identified by TLC and  $^{13}\text{C}$  NMR. The  $^{13}\text{C}$  spectrum revealed that the allylic and doubly allylic signals at 26.98 and 25.42 ppm had reduced in intensity while signals at 31.54 and 32.25 ppm had appeared. This suggests that the methyl linoleate had undergone partial isomerisation during the reaction or work-up.

For  $^1\text{H}$  and  $^{13}\text{C}$  NMR of the 1:1 ene adducts see Appendix 6,  $m/z$  (FAB) 469.32775.  $\text{M}^{++1} \text{C}_{25}\text{H}_{45}\text{N}_2\text{O}_6$  requires 469.32774. The more polar bands from the column could not be identified from  $^1\text{H}$  or  $^{13}\text{C}$  NMR although, in compound (62), the absence of an allylic  $\text{CH}_2$  signal at *ca.* 2 ppm allows the tentative assignment of a tandem ene/Diels-Alder adduct analogous to compounds (50 & 51) (Section 5.4.13),  $m/z$  (FAB) 643.39176.  $\text{M}^{++1} \text{C}_{31}\text{H}_{55}\text{N}_4\text{O}_{10}$  requires 643.39179. The tentatively assigned "other 2:1 adducts" were distinguishable from (62) in their unsaturated proton absorptions as well as in the presence of a signal at 2.0 ppm, but they were not characterised.

## 5.6 Reactions of MTAD

### 5.6.1 2,4,4-Trimethyl-2-pentene

2,4,4-Trimethyl-2-pentene (0.81 g, 7.3 mmol) was stirred with MTAD (0.16 g, 1.4 mmol) in dichloromethane (10 ml) at 0°C until the bright pink colour of the MTAD was discharged. The solvent and excess alkene were removed under vacuum to yield a white solid in almost quantitative yield, (67) (0.32 g, 98%) which recrystallised from cyclohexane, m.p. 142-143°C, (Found: C, 58.38; H, 8.81; N, 18.93.  $C_{11}H_{19}N_3O_2$  requires C, 58.65; H, 8.50; N, 18.65%);  $\delta_H$  (360 MHz) 1.01 (9H, s,  $C(CH_3)_3$ ), 1.77 (3H, d,  $J$  0.6, 2A-H), 2.99 (3H, s, MTAD-Me), 4.40 (1H, s, 3-H), 4.99 and 5.01 (2H, t and s,  $J$  1.4, 1-H), 9.35 (1H, br s, NH);  $\delta_C$  (50 MHz) 23.67 (C-2A), 24.94 (MTAD-Me), 27.49 ( $C(CH_3)_3$ ), 35.16 ( $C(CH_3)_3$ ), 68.27 (C-3), 117.17 (C-1), 140.11 (C-2), 153.64 and 154.85 (C=O).



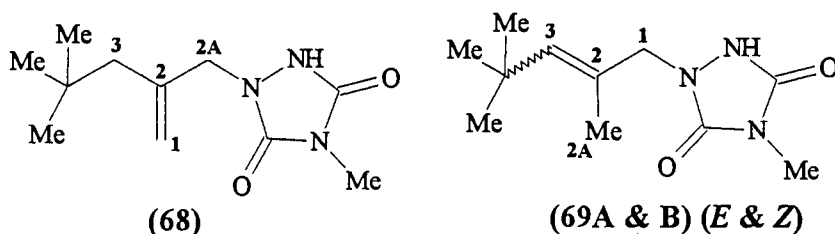
(67)

### 5.6.2 2,4,4-Trimethyl-1-pentene

2,4,4-Trimethyl-1-pentene (0.81 g, 7.3 mmol) was reacted under identical conditions to section 5.6.1 to give a mixture of compounds (68 and 69A & 69B) (0.32 g, 98%). From integral measurements, the ratio of products (68:69A:69B) was 9:1:1. Compound (68) was selectively recrystallised from cyclohexane, m.p. 119.5-120.5°C, (Found: C, 58.68; H, 8.72; N, 18.70.  $C_{11}H_{19}N_3O_2$  requires C, 58.65; H, 8.50; N, 18.65%);  $\delta_H$  (200 MHz) 0.90 (9H, s,  $C(CH_3)_3$ ), 1.90 (2H, s, 3-H), 3.04 (3H, s, MTAD-Me), 4.07 (2H, s, 2A-H), 4.96 and 5.09 (2H, 2xd,  $J$  0.5 and 1.3, 1-H), 9.15 (1H, br s, NH);  $\delta_C$

(50 MHz) 25.02 (MTAD-Me), 29.52 (C(CH<sub>3</sub>)<sub>3</sub>), 31.36 (C(CH<sub>3</sub>)<sub>3</sub>), 46.41 (C-3), 52.43 (C-2A), 117.30 (C-1), 140.16 (C-2), 153.64 and 154.78 (C=O).

*Cis* and *trans* (69) (*ie.* A & B) were not separated. The following NMR data is for the mixture.  $\delta_{\text{H}}$  (360 MHz) 1.04 (2x9H, s, C(CH<sub>3</sub>)<sub>3</sub>), 1.55 and 1.64 (2x3H, 2xd, *J* 1.2, 2A-H), 2.98 (2x3H, s, MTAD-Me), 3.88 and 4.25 (2x2H, s, 1-H), 5.38 and 5.42 (2x1H, 2xd, *J* 1.2, 3-H), 9.3 (2x1H, br s, NH);  $\delta_{\text{C}}$  (50 MHz) 14.77, 22.35 (C-2A), 24.98 (MTAD-Me), 30.36, 31.41 (C(CH<sub>3</sub>)<sub>3</sub>), 31.28, 32.38 (C(CH<sub>3</sub>)<sub>3</sub>), 46.60, 55.98 (C-1), , 126.51, 126.58 (C-2), 141.49, 142.00 (C-3), 154.67 and 154.67 (C=O).



### 5.6.3 Trimethylpentene competition experiment

Trimethyl-1-pentene (0.81 g, 7.3 mmol) and trimethyl-2-pentene (0.81 g, 7.3 mmol) were stirred with MTAD (0.16 g, 1.4 mmol) in dichloromethane (15 ml) until the bright colour of the MTAD had faded. Examination of the crude reaction mixture by <sup>1</sup>H NMR revealed that all the signals for the expected adducts (67, 68, 69A & 69B) were present. Integral expansion was used to estimate the adduct ratio (67:68:69A:69B) as 7:8:1:1.

## 5.6.4 Polyisobutene (PIB)

### 5.6.4.1 Examination of starting materials:

Several samples of polyisobutenes were supplied by Castrol; *Napvis X10*, *Napvis R*, *PIB 450* and *PIB 950* (m wt ca. 160-280, 160-280, 450 and 950 respectively). Examination by  $^1\text{H}$  and  $^{13}\text{C}$  NMR revealed that the samples did not have the theoretical structure of polymerised isobutene (2-methyl-1-pentene).

**Napvis X10:**  $\delta_{\text{H}}$  (360 MHz) 0.7-1.2 (m,  $\text{CH}_3$  envelope), 1.2-1.8 (m,  $\text{CH}_2$  envelope), 1.99-2.2 (m), 2.85 (m), 4.7 (m), 4.85 (m), 5.3 (q), 5.4 (m);  $\delta_{\text{C}}$  (50 MHz) 13-39 [multiple signals including 31.1 ( $-\text{CMe}_2\text{CH}_2-$ ) and 38.1 ( $-\text{CMe}_2\text{CH}_2-$ )], 55-60 [multiple signals including 59.5 ( $-\text{CMe}_2\text{CH}_2-$ )], 110, 114, 123 ( $\text{CH}_2$  from DEPT spectrum), 134.  $m/z$ (FAB) 169 ( $\text{M}^+ + 1$ ) and major peak at 56 (depolymerised to  $\text{C}_4\text{H}_8$ )  $m/z$ (EI) 224.68, 168.04, 57.16.

**Napvis R:**  $\delta_{\text{H}}$  (360 MHz) 0.7-1.1 (m,  $\text{CH}_3$  envelope), 1.1-1.8 (m,  $\text{CH}_2$  envelope), 1.9-2.1 (m), 4.7 (m), 5.2 (m);  $\delta_{\text{C}}$  (50 MHz) 11-37 [multiple signals including 31.4 ( $-\text{CMe}_2\text{CH}_2-$ ) and 37.5 ( $-\text{CMe}_2\text{CH}_2-$ )], 42-56 [multiple signals], 109, 110, ( $\text{CH}_2$  from DEPT spectrum), 120, 122 ( $\text{CH}$  from DEPT spectrum), 134;  $m/z$ (EI) 224.28, 168.04, 57.16.

**PIB450:**  $\delta_{\text{H}}$  (200 MHz) 0.8-1.0 (m), 1.12 (s), 1.17-1.8 (m including signal at 1.4), 1.98 (m), 2.85 (m), 4.7 (m), 5.2 (m);  $\delta_{\text{C}}$  (50 MHz) 14-25 [multiple signals], 27.3 ( $\text{CH}_3$ ), 29.4, 31.2 ( $-\text{CMe}_2\text{CH}_2-$ ), 38.1 ( $-\text{CMe}_2\text{CH}_2-$ ), 59.5 ( $-\text{CMe}_2\text{CH}_2-$ ), unsaturation too weak to detect.

**PIB950:**  $\delta_{\text{H}}$  (200 MHz) 0.8-0.9 (m), 1.0 (m), 1.1 (s,  $-\text{CMe}_2\text{CH}_2-$ ), 1.3 (m), 1.4 (s,  $-\text{CMe}_2\text{CH}_2-$ ), unsaturation not detected;  $\delta_{\text{C}}$  (50 MHz) 31.2 ( $-\text{CMe}_2\text{CH}_2-$ ), 38.1 ( $-\text{CMe}_2\text{CH}_2-$ ), 59.4 ( $-\text{CMe}_2\text{CH}_2-$ ), unsaturation not detected.



#### 5.6.4.2 Modification of Napvis X10 and Napvis R:

For each polymer, the molecular mass was taken as 224. The PIB (0.224 g, 1 mmol) was stirred at 0°C in dichloromethane (10 ml). MTAD (0.113 g, 1 mmol) was dissolved in dichloromethane (5 ml) and added in 1 ml portions. The time taken for the MTAD to fade from bright pink to colourless after each aliquot was added is tabulated below (Table 26). After solvent removal, the resultant mixtures were colourless, slightly translucent, viscous oils.

Table 26

Time for MTAD to decolourise after each aliquot addition /s				
<i>aliquots</i>	<i>1st</i>	<i>2nd</i>	<i>3rd</i>	<i>4th</i>
<b>Napvis R</b>	20	40	120	800
<b>Napvis X10</b>	25	90	1600	-

**Napvis R adduct:**  $\delta_{\text{H}}$  (200 MHz) 0.6-2.0 (*ca.* 40H, br m, CH<sub>3</sub> and CH<sub>2</sub>), 2.9, 3x3.0 (4H, 4xs, MTAD-Me), 4.6 (1H, m), 5.0 (2H, m), 5.2 (1H, s), 9.2 (1H, br s, NH);  $\delta_{\text{C}}$  (90 MHz) 13-55 [50 signals, including 24.9 (MTAD-Me)], 110.0 & 110.2 (CH), 114.0 & 114.2 (CH), 116.8 & 117.0 (CH), 143.7 (quaternary), 153.3, 154.9 (C=O, MTAD);  $m/z$ (FAB) 338, 282 ( $\text{M}^+ + 1$  for  $n=2, 1$ ).

**Napvis X10 adduct:**  $\delta_{\text{H}}$  (200 MHz) 0.7-2.0 (*ca.* 70H, br m, CH<sub>3</sub> and CH<sub>2</sub>), 2x 2.97, 3.03 (4H, 3xs, MTAD-Me), 4.7 (1H, m), 5.1 (2H, m), 5.2 (1H, m), 9.2 (1.6H, br s, NH);  $\delta_{\text{C}}$  (90 MHz) 14-58 [32 signals, including 24.9 (MTAD-Me)], 113, 115 & 117 (CH), 143.8 (quaternary), 153.4, 155.0 (C=O, MTAD);  $m/z$ (FAB) 450, 394, 338, 282 ( $\text{M}^+ + 1$  for  $n=4, 3, 2, 1$ ).

### 5.6.5 Polyalphaolefin (PAO)

PAO (0.42 g, 1 mmol) was stirred with MTAD (0.056 g, 0.5 mmol) in dichloromethane (10 ml) at 0°C. After 100 min, when the pink colour had faded to pale yellow, the solvent was removed and the residue submitted to dry-flash chromatography to yield:

- (i) recovered PAO (49%), identified by TLC
- (ii) 1:1 adducts, tentatively assigned as (**71 & 72**) (96% w.r.t. MTAD);  $m/z$ (FAB) 534.49983.  $M^{++1}$ ,  $C_{33}H_{64}N_3O_2$  requires 534.49982;  $\delta_H$  (360 MHz) 0.83 (t,  $CH_3$ ), 1.1-1.4 (m,  $CH_2$ ), 1.9-1.21 (m), 2.96, 2.97, 2.98, 2.99, 3.01 (5xs, MTAD-Me), 4.5 (m,  $\alpha$ -CHN), 4.94, 4.96, 5.02, 5.07, 5.16 (5x CH signals), 5.36 (m, CH), 9.25 (NH);  $\delta_C$  13.9 ( $CH_3$ ), 22.5 ( $CH_2$ ), 24.5 and 24.8 (MTAD-Me), 29.2, 29.5, 31.7 ( $CH_2$ ), unsaturation too weak to be detected, 155 (C=O).

### 5.6.6 1,4-Pentadiene

1,4-Pentadiene (0.0135 g, 0.2 mmol) was stirred with MTAD (0.023 g, 0.2 mmol) as in the general procedure. The colour faded slowly and the mixture was allowed to stir overnight.  $^1H$  NMR revealed that tandem ene/Diels-Alder adduct had been formed, similar to the analogous PTAD adducts (**50 & 51**) (5.4.11). These compounds were not isolated.

### 5.6.7 Methyl linoleate

Methyl linoleate (0.059 g, 0.2 mmol) was stirred with MTAD (0.023 g, 0.2 mmol) as in the general procedure. The pink colour faded in 21 min. Examination of the resultant mixture by  $^1H$  NMR (360 MHz) revealed, by comparison with the analogous PTAD reaction, that the non-conjugated 1:1 adducts (*cf.* **46 & 47**) and tandem ene/Diels-Alder 2:1 adducts (*cf.* **50 & 51**) were the major products, while the conjugated 1:1 adducts were also formed (*cf.* **48 & 49**). These compounds were not isolated.

## 5.7 Reactions of Formaldehyde

### 5.7.1 General Procedure

All glassware was dried at 140°C for 4 h before use, assembled and flushed with dry N<sub>2</sub>. The alkene and paraformaldehyde were stirred at 0°C in freshly distilled, dry dichloromethane (15 ml). EtAlCl<sub>2</sub> (1.0 M in hexane) was added slowly by syringe through a septum and allowed to stir for 1 h (all under N<sub>2</sub>). Ether (20 ml) was added to quench the reaction, then water (10 ml) was added slowly until gas evolution ceased. The mixture was stirred until the precipitated alumina dissolved. The organic layer was separated and the aqueous layer was washed twice with ether (2x 15 ml). The combined aqueous layer was washed twice with brine, dried over MgSO<sub>4</sub> then evaporated *in vacuo*. The residue was submitted to dry-flash chromatography to recover unreacted alkene, followed by the ene adducts.

### 5.7.2 Oleyl acetate

Oleyl acetate (0.74 g, 2.5 mmol), paraformaldehyde (0.084 g, 2.75 mmol) and EtAlCl<sub>2</sub> (5.5 ml, 5.5 mmol) were reacted as in the general procedure to yield:

- (i) recovered oleyl acetate (7%), identified by TLC
- (ii) 1:1 ene adducts (**31A & B**, 82%); *m/z* (FAB) 341.30558 (M<sup>+</sup> +1, C<sub>21</sub>H<sub>41</sub>O<sub>3</sub> requires 341.30555) *m/z* (FAB) 323.29501 [M<sup>+</sup> +1 (-H<sub>2</sub>O), C<sub>21</sub>H<sub>39</sub>O<sub>2</sub> requires 323.29499];  $\nu_{\max}$  /cm<sup>-1</sup> 3440 (OH), 1742 (C=O), 970 (*trans* C=C). For <sup>1</sup>H and <sup>13</sup>C NMR data see Appendix 12.

### 5.7.3 Methyl oleate

Methyl oleate (0.74 g, 2.4 mmol), paraformaldehyde (0.084 g, 2.75 mmol) and EtAlCl<sub>2</sub> (5.5 ml, 5.5 mmol) were reacted as in the general procedure to yield:

- (i) recovered methyl oleate (33%), identified by TLC and <sup>1</sup>H NMR. Examination by <sup>13</sup>C showed the recovered material to be unisomerised.

- (ii) 1:1 ene adducts (**32A & B**, 63%);  $m/z$  (FAB) 327.28992 ( $M^+ + 1$ ,  $C_{20}H_{39}O_3$  requires 327.28990)  $m/z$  (FAB) 309.27932 [ $M^+ + 1$  ( $-H_2O$ ),  $C_{20}H_{37}O_2$  requires 309.27934];  $\nu_{\max}/\text{cm}^{-1}$  3440 (OH), 1742 (C=O), 970 (*trans* C=C). For  $^1\text{H}$  and  $^{13}\text{C}$  NMR data see Appendix 13.

#### 5.7.4 Jojoba

Three ratios of jojoba:formaldehyde: $\text{EtAlCl}_2$  were reacted as in the general procedure as tabulated below (Table 7):

Table 7

Reactant Ratios			Product Yields		
jojoba	$\text{CH}_2\text{O}$	$\text{EtAlCl}_2$	recovered jojoba	mono-adducts (33)	di-adducts (34)
1.54 g 2.5 mmol	0.082 g 2.75 mmol	5.5 ml 5.5 mmol	54%	30%	8%
1.54 g 2.5 mmol	0.16 g 5.5 mmol	8.25 ml 8.25 mmol	10%	32%	52%
1.55 g 2.5 mmol	0.22 g 7.5 mmol	10.25 ml 10.25 mmol	5%	31%	57%

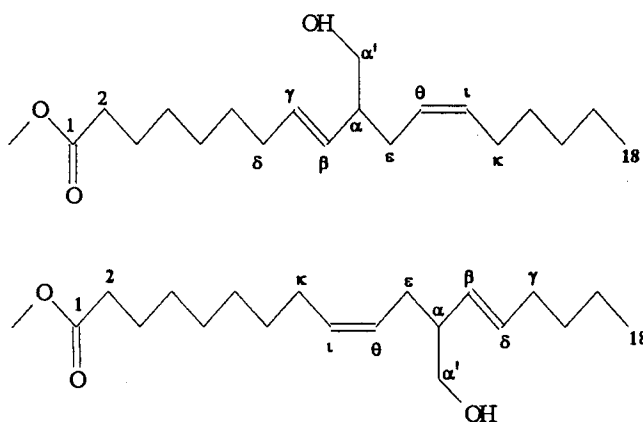
**Mono-adducts (33):**  $m/z$  (FAB) 647.63419 [ $M^+ + 1$ ,  $C_{43}H_{83}O_3$  ( $m+n=21$ ) requires 647.63418], 619.60296 [ $M^+ + 1$   $C_{41}H_{79}O_3$  ( $m+n=19$ ) requires 619.60289], 629.62361 [ $M^+ + 1$ ,  $C_{43}H_{81}O_2$  [ $m+n=21$  ( $-H_2O$ )] requires 629.62362}, 601.59233 [ $M^+ + 1$   $C_{41}H_{77}O_2$  [ $m+n=19$  ( $-H_2O$ )] requires 601.59232];  $\nu_{\max}/\text{cm}^{-1}$  3440br (OH), 1738 (C=O), 969 (*trans* C=C). For  $^1\text{H}$  and  $^{13}\text{C}$  NMR data see Appendices 14 & 15.

**Di-adducts (34):**  $m/z$  (FAB) 641.62367 [ $M^+ + 1$ ,  $C_{44}H_{81}O_2$  [ $m+n=21$  ( $-2x H_2O$ )] requires 641.62362];  $\nu_{\max}/\text{cm}^{-1}$  3367br (OH), 1738 (C=O), 969 (*trans* C=C). For  $^1\text{H}$  and  $^{13}\text{C}$  NMR data see Appendices 14 & 15.

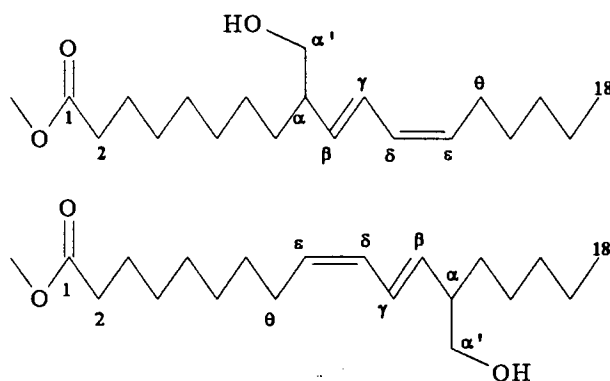
### 5.7.5 Methyl linoleate

Methyl linoleate (0.74 g, 2.5 mmol), paraformaldehyde (0.16 g, 5.5 mmol) and  $\text{EtAlCl}_2$  (8.25 ml, 8.25 mmol) were reacted as in the general procedure to yield:

- (i) recovered methyl linoleate (39%), identified by TLC. Examination by  $^{13}\text{C}$  showed the recovered material had partially isomerised; the intensities of the allylic and doubly-allylic signals had reduced.
- (ii) mono-adducts (63A&B and 64A&B, 46%);  $m/z(\text{FAB})$  307.26368 [ $\text{M}^+ + 1$  ( $-\text{H}_2\text{O}$ ,  $\text{C}_{20}\text{H}_{35}\text{O}_2$  requires 307.26369)]. For  $^1\text{H}$  and  $^{13}\text{C}$  NMR data see Appendix 16. The ratio of 63:64 was *ca.* 9:1 by  $^1\text{H}$  NMR estimation.
- (iii) despite a careful search, no evidence of a 2:1 tandem ene/Diels-Alder adduct product was found.



**63A&B**

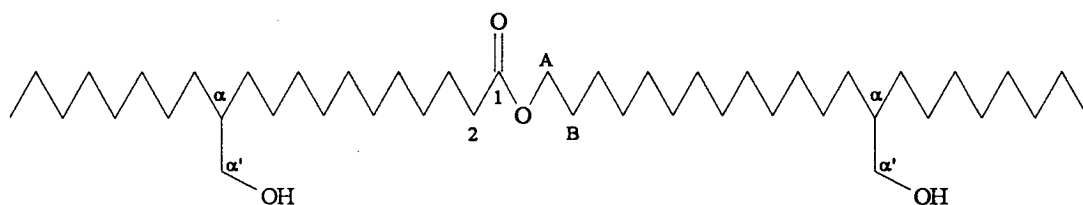


**64A&B**

## 5.8 Modifications of Dihydroxymethyl-Jojoba (DHMJ) (34)

### 5.8.1 Hydrogenation of Dihydroxymethyl-Jojoba (DHMJ) (34)

To a solution of DHMJ (34) (0.057 g, 0.08 mmol) in ethanol was added 10% Pd-C (6 mg). The mixture was degassed under vacuum and allowed to stir under a hydrogen atmosphere for 70 h. A further quantity of Pd-C was added (10 mg) and the hydrogenation was continued for a further 40 h. After filtration to remove the catalyst, a colourless oil was obtained (0.04 g, 70% yield) which was identified by NMR to be fully hydrogenated DHMJ (35A). The alkene absorptions at 5.0 - 5.6 ppm had been removed in the proton spectrum as had those at 131 and 134 ppm in the  $^{13}\text{C}$  NMR spectrum.

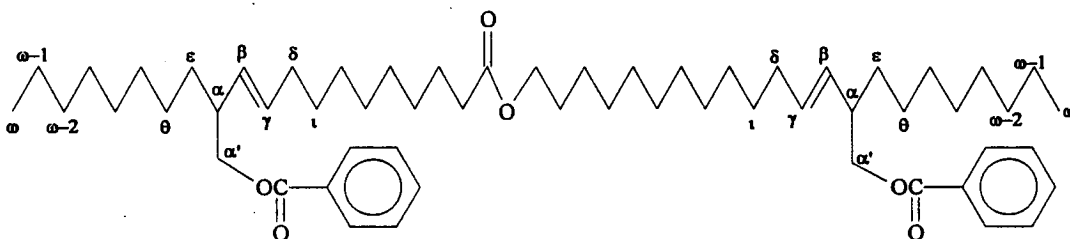


$m/z$  (FAB) 681.67609 ( $\text{M}^++1$ ,  $\text{C}_{44}\text{H}_{89}\text{O}_4$  requires 681.67605).  $\delta_{\text{H}}$  (200 MHz) 0.86 (6H, t,  $J$  6.4,  $\omega$ -H), 1.18 - 1.50 ( $\text{CH}_2$  envelope), 1.59 (4H, m,  $J$  6.8, 3-H and B-H), 1.94 (4H, br s, OH and  $\alpha$ -H), 2.28 (2H, t,  $J$  7.5, 2-H), 3.51 (4H, d,  $J$  5.2,  $\alpha'$ -H), 4.03 (2H, t,  $J$  6.7, A-H).  $\delta_{\text{C}}$  (90 MHz) 13.95 (C- $\omega$ ), 22.53 (C-[ $\omega$ -1]), 24.87 (C-3), 25.78 (C-C), 28.50 (C-B), 29.00 - 29.93 ( $\text{CH}_2$  envelope), 31.76 (C-[ $\omega$ -2]), 34.25 (C-2), 40.37 (C- $\alpha$ ), 64.27 (C-A), 65.51 (C- $\alpha'$ ), 173.92 (C-1).

### 5.8.2 Esterification of Dihydroxymethyl-Jojoba (DHMJ) (34) with Benzoyl Chloride

To a solution of DHMJ (0.12 g, 0.18 mmol) in dry toluene (5 ml) was added two equivalents of benzoyl chloride (0.049 g, 0.36 mmol). The flask was fitted with a reflux condenser and nitrogen gas was bubbled through the solution to remove the HCl gas being formed. The mixture was heated to

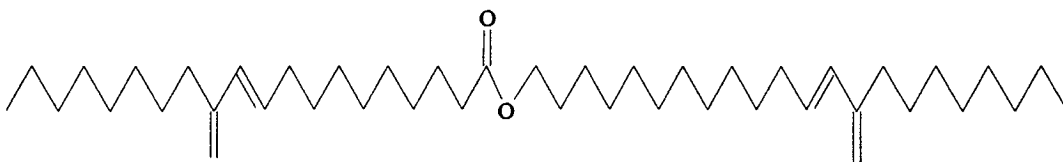
100°C for 4 h and then washed with Na<sub>2</sub>CO<sub>3</sub> (2M) to remove any excess benzoyl chloride. The yield was 0.147 g of the ester (**35B**, 94%).



(**35B**)

$\delta_H$  (200 MHz) 0.87 (3H, m,  $\omega$ -H), 1.26 (CH<sub>2</sub> envelope), 1.61 (4H, B-H and 3-H), 2.00 (4H, q,  $J$  6.4,  $\delta$ -H), 2.28 (2H, t,  $J$  7.5, 2-H), 2.44 (2H, m,  $\alpha$ -H), 4.05 (2H, t,  $J$  6.7, A-H), 4.19 (4H, d,  $J$  6.7,  $\alpha'$ -H), 5.23 (2H, dd,  $J$  15.3, 8.4,  $\beta$ -H), 5.51 (2H, dt,  $J$  15.3, 6.7,  $\gamma$ -H), 7.38 - 7.58 and 8.00 - 8.06 (10H, 2 x m, Ph).  $\delta_C$  (50 MHz) 13.97 (C- $\omega$ ), 22.52 (C-[ $\omega$ -1]), 24.85 (C-3), 25.78 (C-C), 26.78 (tentatively C- $\theta$  or  $\iota$ ), 28.50 (C-B), 28.86 - 29.46 (CH<sub>2</sub> envelope), 31.35 (C- $\epsilon$ ), 31.73 (C-[ $\omega$ -2]), 32.48 (C- $\delta$ ), 34.22 (C-2), 42.06 (C- $\alpha$ ), 64.32 (C-A), 68.07 (C- $\alpha'$ ), 128.11 129.37, 132.60 (Ph), 130.36 (C- $\beta/\gamma$ ) (second alkene signal obscured by Ph absorption), 166.39 (COPh), 173.82 (C-1)

Under FAB mass spectroscopy conditions the molecular ion peak was not detected. However, a fragment consistent with the elimination of two moles of benzoic acid, with a mass of  $M^++1 = 642$  was observed. This fragment is likely to have a highly unsaturated structure similar to (**87**).

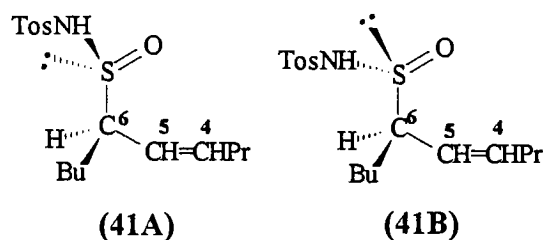


(**87**)

## 5.9 Reactions of *N*-Sulphinyl-*p*-toluenesulfonamide (TosNSO)

### 5.9.1 *Cis*-5-Decene

*Cis*-5-Decene (0.308 g, 2.2 mmol) and TosNSO (0.231 g, 1.1 mmol) were stirred together in dry dichloromethane at  $-30^{\circ}\text{C}$ . The yellow solution was allowed to warm to room temperature and was stirred for 24 h, during which time it became colourless. After removal of solvent, the residue was submitted to dry-flash chromatography to yield, in order of elution: recovered decene (0.131 g, 0.94 mmol), *p*-toluenesulfonamide (0.080 g, 0.44 mmol) and a highly polar adduct (41A & B). This was eluted with 100% ethanol in 41% yield (0.160 g, 0.45 mmol).



$m/z$  (FAB) 358.15106, ( $M^{+}+1$ ,  $\text{C}_{17}\text{H}_{28}\text{NO}_3\text{S}_2$  requires 358.15015).  $\delta_{\text{H}}$  (360 MHz) 0.96 (6H, 2 x m, 1-H and 10-H), 1.40 (6H, m, 2-H, 8-H, 9-H), 2.01 (2H, m,  $\delta$ -H), 2.47 (3H, s, Me[Tos]), 3.05 (1H, m,  $\alpha$ -H), 5.18 and 5.25 (taken together represent 1H), [5.18 (0.4H, ddt,  $J$  15.3, 9.4, 1.3 Hz,  $\beta$ -H), 5.25 (0.6H, ddt,  $J$  15.3, 9.1, 1.3 Hz,  $\beta$ -H)], 5.67 and 5.69 (taken together represent 1H) [5.67 (larger contribution, dt,  $J$  15.4, 6.7 Hz,  $\gamma$ -H), 5.69 (smaller contribution, dt,  $J$  15.4, 7.2 Hz,  $\gamma$ -H)], 7.35 and 7.80 (4H, 2 x d, Ph[Tos]).  $\delta_{\text{C}}$  (50 MHz) 13.48, 13.76 (C-1 and C-10), 21.15 (Me[Tos]), 21.92, 22.34 (C-2 and C-9), 28.64 (C- $\epsilon$ ), 34.52 (C- $\delta$ ), 67.33, 67.93 (C- $\alpha$  [diastereomers]), 122.57, 123.96 (C- $\beta/\gamma$ ), 126.67, 128.67 (*o*, *m*-Ph), 137.86 (C- $\beta/\gamma$  - doubling visible but unresolved), 140.21, 141.04 (*i*, *p*-Ph).



Methyl oleate (0.592 g, 2 mmol) and TosNSO (0.434 g, 2 mmol) were stirred under N<sub>2</sub> at 0°C in dry dichloromethane for 24 h. The resultant mixture was submitted to dry flash column chromatography to yield, in order of elution:

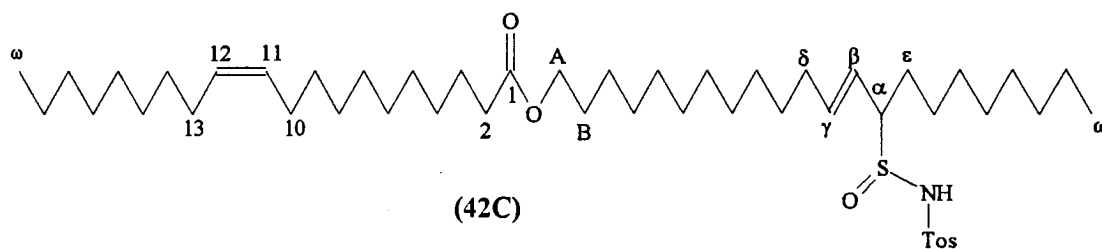
- (i) recovered methyl oleate (26%). Examination by  $^{13}\text{C}$  NMR revealed that *ca.* 80% of the *cis* double bonds had isomerised to the thermodynamically more stable *trans* geometry. This was estimated by comparison of the allylic  $\text{CH}_2$  signal intensities (at 26.98 and 32.37 ppm) and was also visible in the alkene CH peaks.
- (ii) *p*-toluene sulfonamide (42% w.r.t. TosNSO) as a by-product. This was identified by TLC and melting point (125 -129°C)
- (iii) ene adducts (**42A & B**) (0.461 g, 45%)  $\delta_{\text{H}}$  (200 MHz) 0.84 (3H, m, 18-H), 1.17 - 1.30 ( $\text{CH}_2$  envelope), 1.53 (2H, q, 3-H), 1.80 (2H, br,  $\delta$ -H), 2.24 (2H, t, 2-H), 2.31 (3H, s, Me[Tos]), 3.63 (1H, m,  $\alpha$ -H), 3.63 (3-H, s, OMe), 4.7 (1H, br s, NH), 5.0 (1H, m,  $\beta$ -H), 5.5 (1H, m,  $\gamma$ -H), 7.07 and 7.70 (4H, 2 x d, Ph[Tos]).  $\delta_{\text{C}}$  (90 MHz) 13.87 (C-18), 21.10 (Me[Tos]), 22.44 (C-17), 24.69 (C-3), 28.62 - 29.52 ( $\text{CH}_2$  envelope), 31.71 (C-16), 32.35 and 32.49 (C- $\delta$ ), 33.80 (C-2), 51.23 (OMe) 67.45 and 68.30 (C- $\alpha$ ), 122.4 and 123.0 (C- $\beta/\gamma$ ), 126.50 and 128.63 (Ph[Tos]), 138.1 (C- $\beta/\gamma$ , doubling visible but unresolved), 174.07 (C-1)



### 5.9.3 Jojoba Oil

Jojoba oil (0.616 g, 1 mmol) and TosNSO (0.434 g, 2 mmol) were stirred under nitrogen in dry dichloromethane at 0°C for 24 h. The crude reaction mixture was submitted to dry-flash chromatography (silica, hexane/ether/ethanol) to yield, in order of elution:

- (i) recovered jojoba (40 %). No isomerisation was detectable by  $^{13}\text{C}$  NMR.
- (ii) *p*-toluenesulfonamide (38% based on TosNSO) as a byproduct. This was identified by comparison with an authentic TLC sample and with previous experiments.
- (iii) ene mono and di-adducts in a combined yield of 53%. Further purification was only partially successful and a sample of the mono-adduct (42C) was analysed by  $^1\text{H}$  and  $^{13}\text{C}$  NMR.



$\delta_{\text{H}}$  (200 MHz) 0.84 (6H, m,  $\omega$ -H), 1.16 - 1.30 ( $\text{CH}_2$  envelope), 1.58 (4H, m, 3-H and B-H), 1.79 (2H, br s,  $\delta$ -H), 1.98 (4H, quin, residual *cis* allylic protons), 2.27 (2H, t, 2-H), 2.29 (3-H, s, Me[Tos]), 3.09 (1H, br,  $\alpha$ -H), 4.03 (2H, t, A-H), 4.79 (1H, br s, NH), 4.99 (1H, br,  $\beta$ -H), 5.32 (2H, t,  $J$  5.2, residual *cis* alkene protons), 5.47 (1H, br,  $\gamma$ -H), 7.04 and 7.71 (4H, 2 x d, Ph[Tos]).  $\delta_{\text{C}}$  (50 MHz) 13.96 (C- $\omega$ ), 22.53 (C-[ $\omega$ -1]), 24.83 (C-3), 25.79 (C-C), 27.02 (residual *cis* allylics), 28.49 (C-B), 29.14 - 29.58 ( $\text{CH}_2$  envelope), 31.78 (C-[ $\omega$ -2]), 32.60 (C- $\delta$ ), 34.18 (C-2), 64.22 (C-A), 67.99 (C- $\alpha$ ), 122.53, 123.95 (C- $\beta/\gamma$ ), 126.70, 128.64 (Ph[Tos]), 129.69 (residual *cis* alkenes), 138.18 (C- $\beta/\gamma$ ), 140.42 140.78 (Ph[Tos]), 173.78 (C-1).

## 5.10 Kinetics Experiments

### 5.10.1 UV/Visible Spectral Monitoring of Enophile Disappearance

#### 5.10.1.1 PTAD with methyl oleate, methyl elaidate, jojoba and *trans*-jojoba

For each case, solutions of the alkenes (1 ml) and PTAD (2 ml, *ca.* 7 mmol) in dichloromethane at  $22 \geq T \geq 21^\circ\text{C}$  were mixed in a 1-cm UV cell. The PTAD absorption at  $\lambda_{\text{max}}$  (543 nm) in the visible region was measured *vs.* time. The alkene concentration was *ca.* 10x in excess of the PTAD concentration and therefore a pseudo first order rate equation was used (Equation 9).

$$\ln [(A_t - A_\infty)/(A_0 - A_\infty)] = -k_1't \quad \text{Equation 9}$$

where:

$A_t$  = absorbance at time  $t$

$A_\infty$  = final absorbance

$A_0$  = initial absorbance

$k_1'$  = pseudo first order rate constant

$k_2$  = second order rate constant ( $k_1'$ /initial alkene concentration)

$k_1'$  was found from the gradient of graphs of  $\ln [(A_t - A_\infty)/(A_0 - A_\infty)]$  *vs.* time. From  $k_1'$ , the second order rate constant ( $k_2$ ) was calculated by dividing by the initial concentration of the excess alkene. Table 27 shows the  $k_2$  values found. Jojoba and *trans*-jojoba appear to be twice as fast because each mole contains two double bonds in comparison to the model alkenes.

Table 27

alkene	$k_2 / \text{M}^{-1}\text{s}^{-1}$
methyl oleate	1.08
methyl elaidate	0.399
jojoba	1.88
<i>trans</i> -jojoba	0.828

### 5.10.1.2 DEAD with methyl oleate, methyl elaidate

Each of the alkenes (2.96 g, 10 mmol) was dissolved in 10 ml dichloroethane, a solution of DEAD (0.174 g, 1 mmol) in dichloroethane was added and the mixtures were heated under reflux at 83°C for 28 h. The DEAD absorption was monitored by removing 0.5 ml of the mixture at regular intervals, quenching the reaction by adding 2.5 ml of dichloroethane and scanning the visible region 350-500 nm vs. time. Using the same method as above (5.10.1.1)  $k_2$  was calculated for the reactions;

methyl oleate -  $7.6 \times 10^{-5} \text{ M}^{-1}\text{s}^{-1}$ , methyl elaidate -  $17.2 \times 10^{-5} \text{ M}^{-1}\text{s}^{-1}$ .

### 5.10.2 Capillary GC monitoring of alkene disappearance

#### 5.10.2.1 Methyl oleate and elaidate with DEAD

A mixture methyl oleate (0.148 g, 0.5 mmol), methyl elaidate (0.148 g, 0.5 mmol) and methyl palmitate (0.07 g, 0.27 mmol - as internal standard) was made up to 50 ml as a standard solution in trichloroethane. A portion (10 ml) of this solution was refluxed with DEAD (0.348 g, 2 mmol) at 75°C for 31 h. Samples were removed and injected into the GC at 30 min intervals. The disappearance of the methyl oleate and elaidate peaks w.r.t. the standard palmitate peak was monitored with time. The DEAD concentration was in 10x excess over the total alkene concentration and a pseudo first order rate equation was used (Equation 10).

$$\ln \{[\text{alkene}]_t/[\text{alkene}]_0\} = -k_1't \quad \text{Equation 10}$$

where:

$[\text{alkene}]_t$  = area of alkene peak at time,  $t$

$[\text{alkene}]_0$  = area of alkene peak at time zero

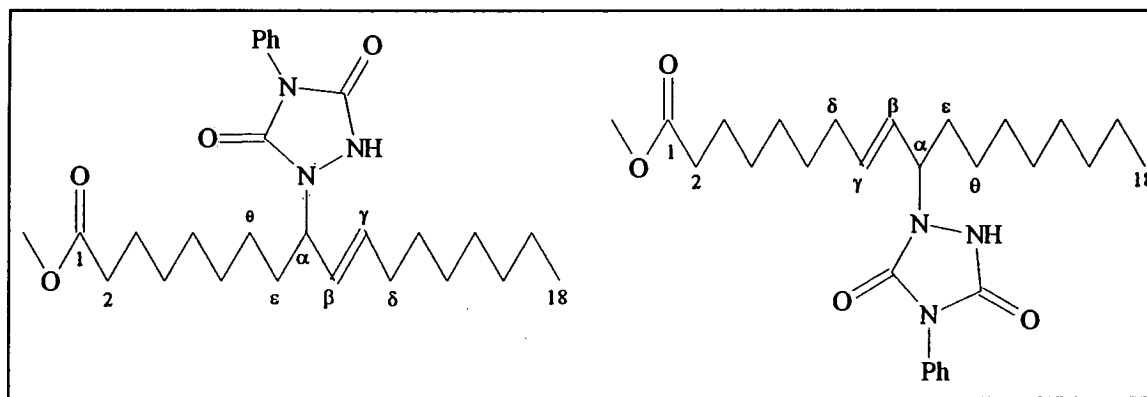
$k_1'$  = pseudo first order rate constant

$k_2$  (second order rate constant) =  $k_1'/[\text{DEAD}]_0$

Graphs of Equation 10 were plotted and from them the second order rate constants ( $k_2$ ) were calculated: methyl oleate -  $6.9 \times 10^{-5} \text{ M}^{-1}\text{s}^{-1}$ , methyl elaidate -  $14.5 \times 10^{-5} \text{ M}^{-1}\text{s}^{-1}$ .

#### **5.10.2.2      Attempted monitoring of methyl oleate and methyl elaidate with PTAD**

A similar standard solution to the above (5.10.2.1) was made up in dichloromethane. A portion was removed and an excess of PTAD was added. The reaction was complete within one minute and so the alkene disappearance could not be measured by this method. The reaction was repeated at  $0^\circ\text{C}$  and under 50x more dilute conditions but the reaction was still too fast to measure.

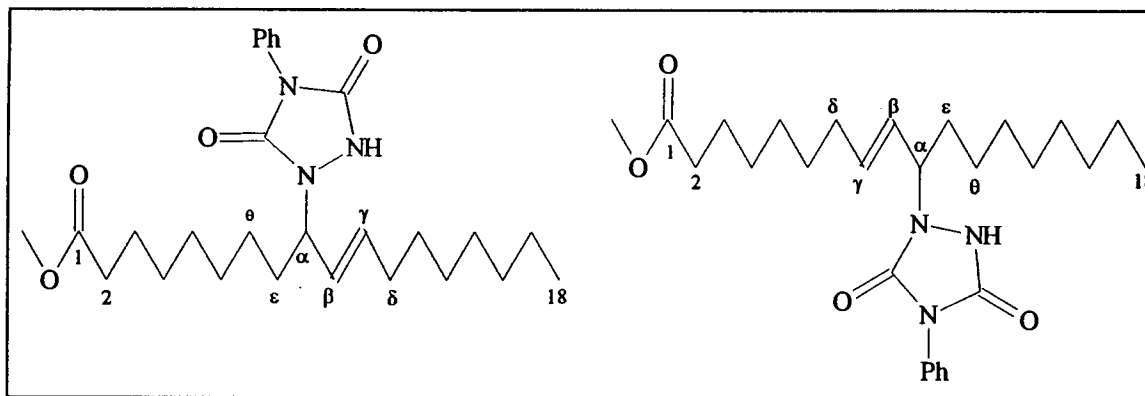


**methyl oleate/PTAD (13A & B)**

$\alpha$	$\beta$	$\gamma$	$\delta$	$\epsilon$	1	2	3	16	17	18	OMe	Ph	others
$\delta_H/ppm, m, J/Hz$ (360 MHz)													
4.53	5.40	5.71	1.95	1.69	-	2.25	1.55	b	b	0.83	3.62	7.25-7.51	CH <sub>2</sub> envelope
q	ddt	dtd	q	2xm <sup>a</sup>		t	quin			t	s	m	1.20-1.25, m
7.5	15.4, 7.5, 1.0	15.4, 7.7, 0.7	6.9			7.4	7.3			6.8			NH 9.50, br s
										0.84			
										t			
										7.1			
$\delta_C/ppm$ (90 MHz)													
58.49	125.61	135.44	ca.	b	174.05	33.74	24.56	31.55	22.38	13.83	51.20	125.17	CH <sub>2</sub> envelope
58.51	125.82	135.77	31.8									127.72	28.35-29.17,
												128.69	C-O 25.70, 25.80,
												131.17	C=O 152.12,
													152.15, 153.75

a: diastereotopic signals; b: within CH<sub>2</sub> envelope

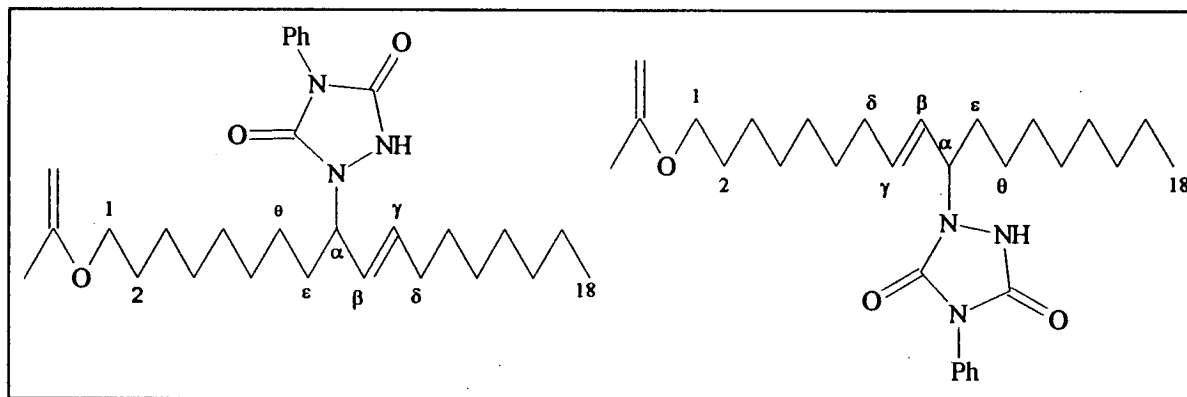
## Appendix 1



methyl elaidate/PTAD (13A & B)													
α	β	γ	δ	ε	1	2	3	16	17	18	OMe	Ph	others
$\delta_H$ /ppm, m, J/Hz (360 MHz)													
4.54	5.41	5.71	1.96	1.67	-	2.25	1.56	b	b	0.841	3.62	7.25-7.50	CH <sub>2</sub> envelope
q	dd	dt	q	2xm <sup>a</sup>		t	quin			t	s	m	1.21-1.24, m
7.5	15.5, 7.5	15.0, 6.9	6.9			7.5	7.1			6.6			NH 9.54, br s
4.55										0.839			
q										t			
7.6										6.6			
$\delta_C$ /ppm (90 MHz)													
58.45	125.56	135.43	ca.	b	174.04	33.72	24.54	31.52	22.36	13.81	51.19	125.15	CH <sub>2</sub> envelope
	125.78	135.77	31.8									127.71	28.33-29.14,
												128.68	C-O 25.67, 25.78,
												131.14	C=O 152.08,
													152.12, 153.75

a: diastereotopic signals; b: within CH<sub>2</sub> envelope

## Appendix 2

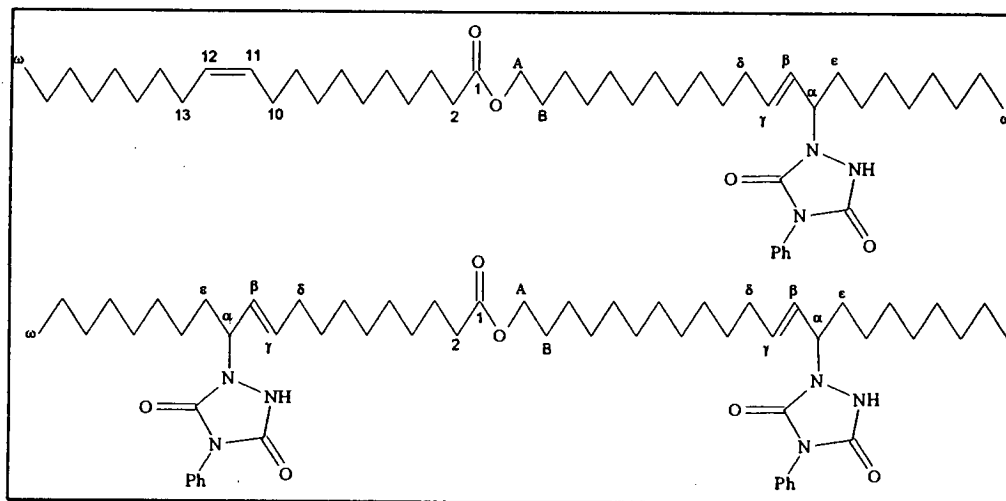


oleyl acetate/PTAD													
$\alpha$	$\beta$	$\gamma$	$\delta$	$\epsilon$	1	2	3	16	17	18	OCOMe	Phenyl	others
$\delta_H$ /ppm, m, J/Hz (200 MHz)													
4.54	5.40	5.72	1.96	ca.	4.00	1.56	b	b	b	0.83	2.00	7.25-7.51	CH <sub>2</sub> envelope
q	dd	dt	q	1.7 <sup>a</sup>	t	m				t	s	m	1.21-1.23, m
7.4	15.4, 7.4	15.2, 6.8	6.7		6.6					6.4			NH 9.50, br s
$\delta_C$ /ppm (50 MHz)													
58.49	125.60	135.52	31.75	ca.	64.32	28.28	25.55	31.53	22.36	13.80	20.70	125.14	CH <sub>2</sub> envelope
	125.77	135.77	32.00	32.1								127.69	28.50-29.14,
												128.66	C-O 25.76,
												131.20	C=O 171.04 (lipid),
													152.13, 153.75

a: overlapping 2-H; b: within CH<sub>2</sub> envelope

### Appendix 3

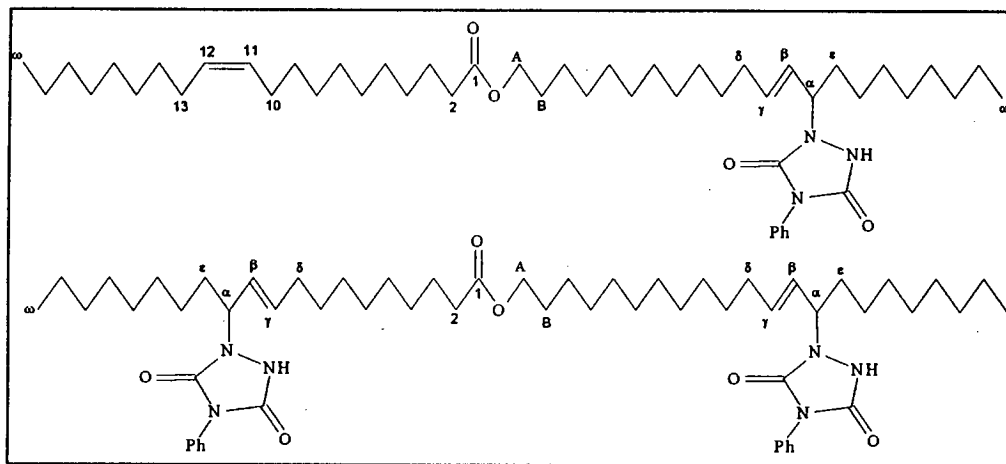




$\delta_{\text{H}}/\text{ppm}$ , m, $J/\text{Hz}$ (360 MHz)								
$\alpha$	$\beta$	$\gamma$	$\delta$	$\epsilon$	11, 12	10, 13	others	
jojoba/PTAD (monoadduct) (15)								
4.56	5.42	5.73	1.98	ca. 1.7 <sup>a</sup>	5.32	1.98	H(A) 4.04, t, 6.7	CH <sub>2</sub> envelope
q	dd	dt	m		t	m	H(B&3) 1.59, m	1.22-1.24, m
7.6	15.4, 7.5	15.4, 6.8			4.7		H(2) 2.27, t, 7.5	N-H 9.0, br s
							$\omega$ -H 0.85,0.86, 2xt, 6.7	Ph 7.30-7.52
jojoba/PTAD (diadduct) (16)								
4.57	5.43	5.75	1.99	ca. 1.7 <sup>a</sup>	b	b	H(A) 4.05, t, 6.7	CH <sub>2</sub> envelope
m	dd	dt	q				H(B&3) 1.59, quin, 6.2	1.23-1.27, m
	15.4, 7.3	15.4, 6.7	7.0				H(2) 2.27, t, 7.4	N-H 9.0, br s
							$\omega$ -H 0.86,t, 6.8	Ph 7.32-7.52

a: diastereotopic and overlapping H(B); b: *cis*-unsaturation removed by ene reaction

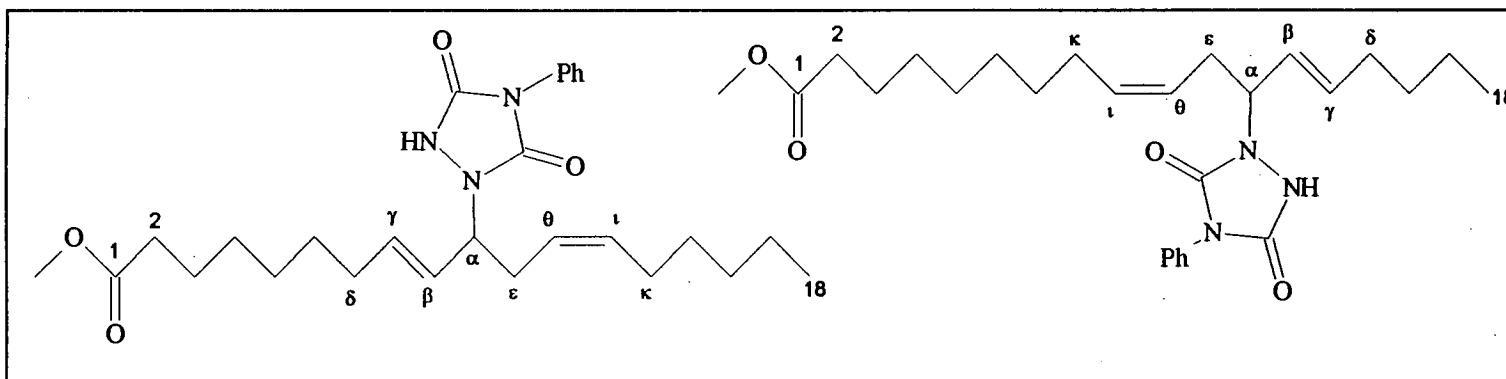
## Appendix 4



$\delta_{\text{C}}/\text{ppm}$ (90 MHz)								
$\alpha$	$\beta$	$\gamma$	$\delta$	$\epsilon$	11, 12	10, 13	others	
jojoba/PTAD (monoadduct) (15)								
58.60	125.73	135.85	31.67	a	129.70	27.04	C(A) 64.25 C(1) 173.87 C(2) 34.20 C(3) 24.83 C( $\omega$ ) 13.95	CH <sub>2</sub> envelope 28.48-29.60 C=O 152.24, 153.89 Ph 125.21, 127.77, 128.76, 131.30
jojoba/PTAD (diadduct) (16)								
58.41	125.55	135.55	31.43	a	b	b	C(A) 64.05 C(1) 173.68 C(2) 33.95 C(3) 24.59 C( $\omega$ ) 13.73	CH <sub>2</sub> envelope 28.24-29.13 C=O 151.99, 153.53 Ph 125.04, 127.55, 128.53, 131.05

a: within CH<sub>2</sub> envelope; b: *cis*-unsaturation removed by ene reaction

## Appendix 5

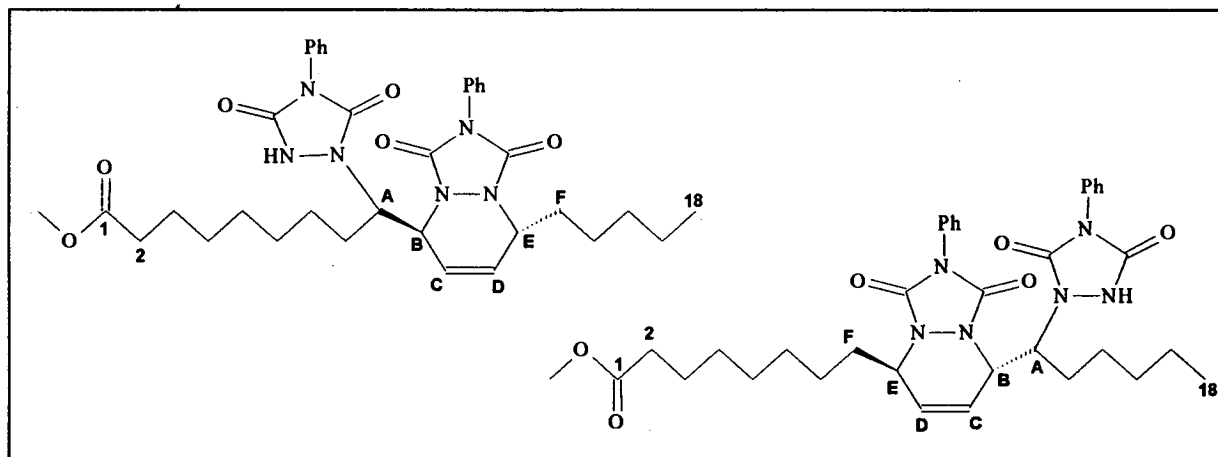


methyl linoleate/PTAD (1:1 adducts) (46 & 47)

$\alpha$	$\beta$	$\gamma$	$\delta$	$\epsilon_A$	$\epsilon_B$	$\theta$	$\iota$	$\kappa$	1	2	3	16	17	18	OMe	Ph	others
$\delta_H$ /ppm, m, J/Hz (360 MHz)																	
4.65	5.43	5.74,	1.96	2.35 <sup>a</sup>	2.54 <sup>a</sup>	5.30	5.45 <sup>b</sup>	1.96	-	2.25	1.56	-	-	0.82,	3.61	7.29-	CH <sub>2</sub> envelope
q	dd	5.75	m	dddd	dddd	dt	m	m		t	m			0.83	s	7.48	1.24-1.39
6.8	15.5,	2x dtd		$\epsilon_A\epsilon_B$ 15	$\epsilon_B\epsilon_A$ 15	$\theta\iota$ 10				7.6				2x t			NH, 9.25, br s
	7.0	15.0, 7.0,		$\epsilon_A\theta$ 8.0	$\epsilon_B\theta$ 6.5	$\theta\epsilon$ 7.5								7.0			
		0.6		$\epsilon_A\alpha$ 8.0	$\epsilon_B\alpha$ 6.0												
				$\epsilon_A\iota$ <1	$\epsilon_B\iota$ <1												
$\delta_C$ /ppm (50 MHz)																	
57.80	124.95	134.95	31.29	30.24		123.42	132.66	26.64	173.66	33.34	24.20	30.76	21.46	13.19	50.79	124.78	CH <sub>2</sub> envelope
57.84		135.17	31.48			123.53	132.82						21.87	13.37		127.33	27.88-29.69
																128.30	C=O 151.94,
																130.72	153.23,

a: diastereotopic signals; b: concealed by  $\beta$

## Appendix 6

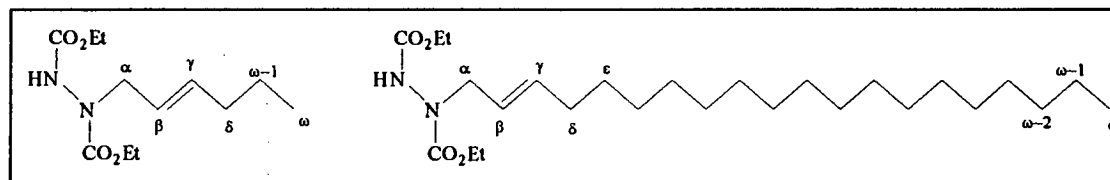


methyl linoleate/PTAD (2:1 adducts) (50 & 51)														
A	B	C	D	E	F	G	1	2	3	16	17	18	OMe	Others
$\delta_H$ /ppm, m, J/Hz (360 MHz)														
4.36 m	4.59 dd 9.6, 4.8	5.91 dd 10.8, 5.0	ca. 6 <sup>a</sup>	4.55 m	1.78 m	1.67 m	-	2.25 m	1.57 m	b	b	b	3.62	Ph 7.18-7.47 NH 9.0 CH <sub>2</sub> env.
(4.85,m)	(4.65,m)	(ca. 6 <sup>a</sup> )	(ca. 6 <sup>a</sup> )	(4.45,m)										
$\delta_C$ /ppm (50 MHz)														
53.63, 54.04, 54.41, 54.65, 55.65, 56.90 c		119.10, 121.76		c	b	b	173.78	33.53	24.37	31.15	21.93	13.51	51.02	Ph (9 signals) 125.14-130.73 C=O (7 signals) 151.75-153.42

Bracketed signals are from the major diastereomer. Diastereomer ratio is 6:5.

a: area contains 3 overlapping alkene signals; b: within CH<sub>2</sub> envelope; c: Carbon signals A, B & E are not distinguished

## Appendix 7

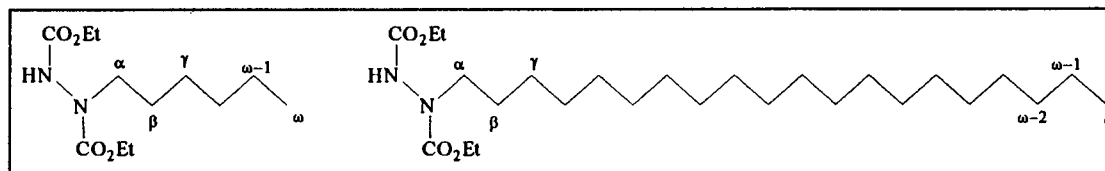


$\delta_H/\text{ppm, m, J/Hz}$													
starting alkene (field strength)	$\alpha$	$\beta$	$\gamma$	$\delta$	$\epsilon$	$\text{CH}_2$ env.	$\omega-2$	$\omega-1$	$\omega$	DEAD $\text{CO}_2\text{CH}_2\text{CH}_3$	DEAD $\text{CO}_2\text{CH}_2\text{CH}_3$	Others	% <i>cis</i> geometry
1-hexene (200 MHz)	3.98	5.37	5.55	1.94	-	-	-	1.30	0.82	4.11	1.19	NH	
	d	dt	dt	q				quin	t	q	t	6.81	
	6.2	15.3,	15.3,	6.9				7.4	7.3	7.1	7.2	br s	
1-octene <sup>a</sup> (80 MHz)	3.95	6.4, 1.1	6.3, 0.9	1.94	-	c	-	c	0.80	4.13	1.18	NH	
	d	ca 5.45 <sup>b</sup> m	ca 5.45 <sup>b</sup> m	q					t	q	t	6.71	
										7.1	7.1	br s	
$\delta_C/\text{ppm (50 MHz)}$													
1-hexene	51.79	123.29	134.10	28.89	21.89	-	-	-	13.28	61.52	14.17	C=O	18%
		123.63	135.07	33.99	22.34					62.09		155.92	
1-octene	51.82	123.05	134.38	26.88	28.45	-	31.04	22.20	13.71	61.55	14.18	C=O	18%
		123.38	135.40	31.92	28.91					62.11		155.95	
1-decene	51.93	123.39 <sup>d</sup>	134.55	27.03	28.89	28.89	31.59	22.43	13.86	61.67	14.27	C=O	18%
			135.55	32.04	29.34					62.21		155.96	
1-dodecene	51.84	123.40 <sup>d</sup>	134.31	26.94	ca. 29 <sup>d</sup>	28.85-	31.59	22.37	13.78	61.50	14.17	C=O	19%
			135.34	31.97		29.25				62.08		155.90	
1-tetradecene <sup>e</sup>	51.83	123.39 <sup>d</sup>	135.36 <sup>d</sup>	26.96	ca. 29 <sup>d</sup>	28.87-	31.63	22.39	13.80	61.52	14.18	C=O	16%
				31.98		29.35				62.09		155.92	

a: 1-octene to 1-eicosene adducts are identical to the above, except that the  $\text{CH}_2$  envelope intensity increases. At 80 MHz the coupling constants cannot be measured.

b:  $\beta$  and  $\gamma$  overlap; c: concealed by  $\text{CO}_2\text{CH}_2\text{CH}_3$ ; d: not resolved; e: 1-hexadecene, octadecene and eicosene adducts are similar (60 MHz).

## Appendix 8

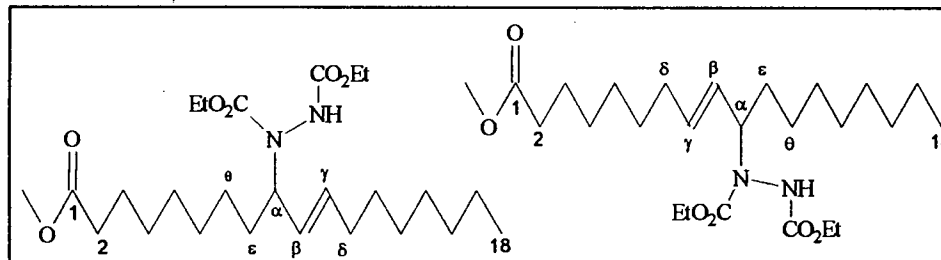


$\delta_H$ /ppm, m, J/Hz (200 MHz)						
hydrogenated adduct of:	$\alpha$	$\beta$	$\omega$	$CH_2$ env. & DEAD $CH_3$	DEAD $OCH_2CH_3$	NH
1-hexene	3.40, t, 7.2	1.48, quin, 6.6	0.79, t, 6.5	1.10-1.27, m	4.08, q, 7.1 4.10, q, 7.1	7.25, br s
1-decene	3.43, t, 7.1	1.51, quin, 6.8	0.83, t, 7.0	1.14-1.26, m	4.12, q, 7.1 4.14, q, 7.1	7.26, br s
1-tetradecene <sup>a</sup>	3.45, t, 7.0	1.5 <sup>b</sup>	0.85, t, <i>ca.</i> 6	1.20-1.29, m	4.14, q, 7.1 4.16, q, 7.1	6.53, br s
1-octadecene <sup>a</sup>	3.42, t, 7.0	1.50 <sup>b</sup>	0.82, t, 6.6	<i>ca.</i> 1.2, m	4.12, m	6.91, br s

a: 80 MHz; b: unresolved at 80 MHz

$\delta_C$ /ppm (50 MHz)										
hydrogenated adduct of:	$\alpha$	$\beta$	$\gamma$	$CH_2$ envelope	$\omega-2$	$\omega-1$	$\omega$	DEAD $OCH_2$	DEAD $OCH_2CH_3$	C=O
1-hexene	49.77	27.01	25.99	-	31.24	22.31	13.74	61.61, 62.03	14.20	156.23
1-decene	49.84	27.13	26.40	29.12-29.37	31.68	22.47	13.91	61.71, 62.12	14.28	156.18
1-tetradecene	49.74	27.04	26.31	29.06-29.36	31.62	22.38	13.79	61.52, 61.97	14.16	156.24
1-octadecene	49.85	27.17	26.44	29.18-29.51	31.75	22.51	13.93	62.14, 61.75	14.30	156.15

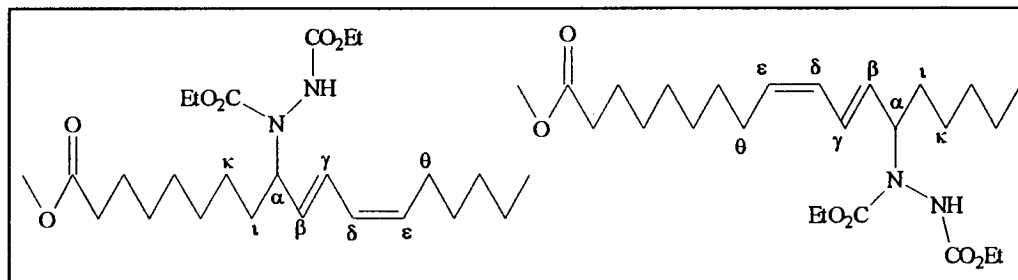
## Appendix 9



methyl oleate /DEAD (23)											
$\alpha$	$\beta$	$\gamma$	$\delta$	$\epsilon$	1	2	3	18	OMe	CH <sub>2</sub> env.	others
$\delta_H$ /ppm, m, J/Hz (360 MHz)											
4.46	5.34	5.57	1.96	1.44	-	2.256	1.57	0.836	3.62	1.20-1.25	DEAD: (CH <sub>3</sub> <sup>a</sup> CH <sub>2</sub> 4.14, q, 7.1) NH 6.27, br s
m	dd	dt	q	m		2.259	quin	0.839	s		
	15.0, 7.3	15.0, 6.5	6.9			2xt	7.0	2xt			
						7.2		7.0			
$\delta_C$ /ppm, (90 MHz)											
59.84	133.39	127.46	32.05	31.51	174.11	33.84	24.67	13.89	51.24	28.11-29.34	C(0) 25.89, 25.99
	133.77	127.72	32.20								C(16) 31.66
											C(17) 22.46
											DEAD:
											(CH <sub>3</sub> 14.25, 14.32
											CH <sub>2</sub> 61.67, 62.08
											C=O 155.92, 156.42)

a: within CH<sub>2</sub> envelope

## Appendix 10

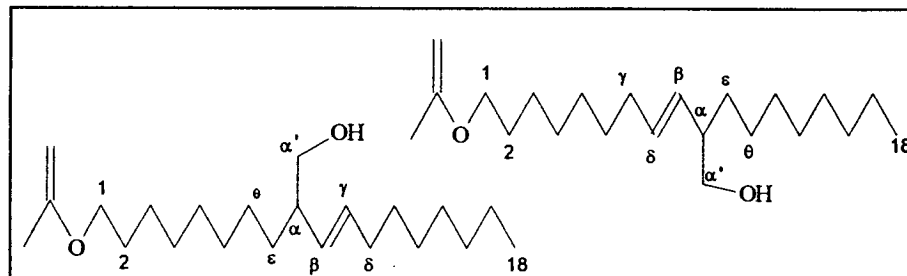


methyl linoleate/DEAD (61)										
$\alpha$	$\beta$	$\gamma$	$\delta$	$\epsilon$	$\theta$	$\iota$	$\kappa$	others	DEAD	
$\delta_H$ /ppm, m, J/Hz (360 MHz)										
4.59	5.56	6.40	5.90	5.43,	2.13	a	a	H(2) 2.267, 2.273	H(3) 1.57, m	$OCH_2$ 4.15, q, 6.8
m	dd	dd	t	5.40	q			2x t, 7.5	OMe 3.6, s	$OCH_2CH_3$ a
	15.1,	15.0,	11.0	2x dt	7.1			H(18) 0.85, 0.86	$CH_2$ env.	
	7.8	11.3		10.0, 7.2				2x t, 6.9	1.21-1.37	
								NH 6.26, br s		
$\delta_C$ /ppm (90 MHz)										
59.70	130.45	127.53	127.62	132.46	27.40	31.09	25.48	C(1) 173.96	C(18) 13.72	$OCH_2$ 61.53, 61.97
				132.68			25.71	C(2) 33.70	OMe 51.10	$OCH_2CH_3$ 14.11, 14.18
								C(3) 24.55	CH env.	C=O 155.69, 156.41
								C(16) 31.38, 31.31	28.75-29.16	
								C(17) 22.23		

a: within  $CH_2$  envelope

## Appendix 11

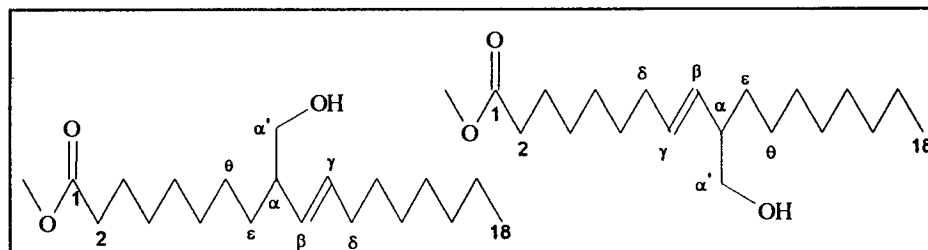




oleyl acetate/formaldehyde (31A&B)												
α	β	γ	δ	ε	α' <sub>A</sub>	α' <sub>B</sub>	OH	1	2	18	OCO <i>Me</i>	others
δ <sub>H</sub> /ppm, m, J/Hz (360 MHz)												
2.07	5.084	5.450	1.96	a	3.28	3.435	1.83 br	3.980	1.55	0.812	1.97	CH <sub>2</sub> env.
m	5.097	5.455	q		dd	3.439	s	3.983	quin	0.815	s	1.10-1.35
	2x ddt	2x dt	7.0		10.4, 8.1	2x dd		2x t	6.7	2x t		
	15.3, 7.4, 1.4	15.3, 6.7				10.4, 5.3		6.7				
δ <sub>C</sub> /ppm (90 MHz)												
45.64	131.05	133.24	32.37	31.85	65.74	-		64.36	28.31	13.84	20.70	CH <sub>2</sub> env.
	131.24	133.49	32.42									28.71-29.41
												C-3 25.62
												C-16 31.61
												C-17 22.40
												C=O 170.97
												26.83

a: within CH<sub>2</sub> envelope

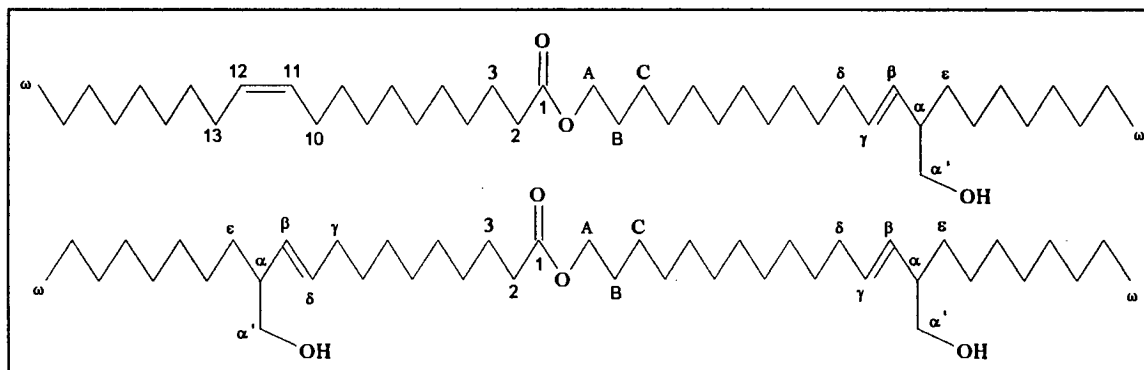
## Appendix 12



methyl oleate/formaldehyde (32A & B)												
$\alpha$	$\beta$	$\gamma$	$\delta$	$\epsilon$	$\alpha'_A$	$\alpha'_B$	OH	1	2	18	OMe	others
$\delta_H/\text{ppm, m, J/Hz (360 MHz)}$												
2.11	5.099	5.494	2.00	a	3.298	3.485	1.58	-	2.270	0.850	3.63	CH <sub>2</sub> env.
m	5.108	5.505	q		3.302	3.491	br s		2.276	0.854	s	1.10-1.35
	2x ddt	2x dtd	6.7		2x dd	2x dd			2x t	2x t		3-H <sup>b</sup>
	15.3, 8.9, 1.4	15.3, 6.3, 0.6			10.4, 8.5	10.4, 5.1			7.4	6.8		
$\delta_C/\text{ppm (90 MHz)}$												
45.63	131.03	133.14	32.31	30.87	65.75	-	174.01	33.78	13.84	51.15		CH <sub>2</sub> env.
	131.30	133.50	32.43									28.85-29.43
												C-3 24.64
												C-16 31.62
												C-17 22.41
												26.77, 26.85
												28.44, 28.67

a: within CH<sub>2</sub> envelope; b: concealed by OH

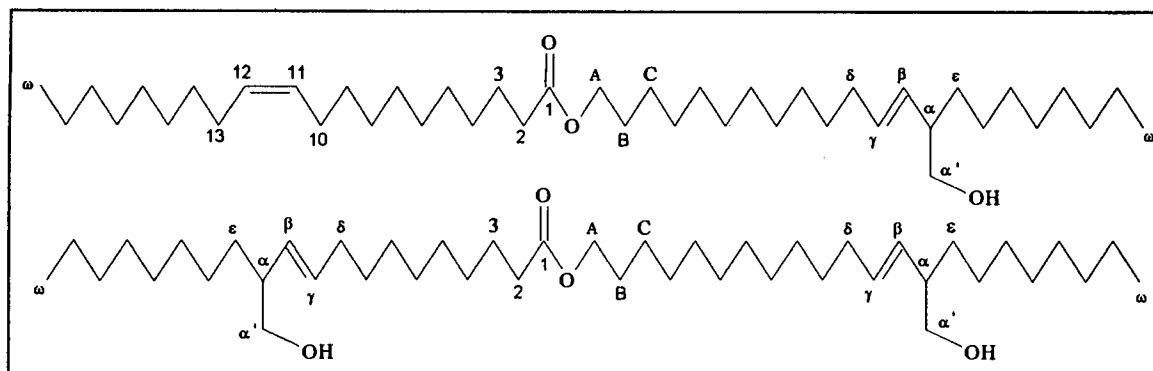
## Appendix 13



$\delta_{\text{H}}/\text{ppm, m, J/Hz (360 MHz)}$											
$\alpha$	$\beta$	$\gamma$	$\delta$	$\epsilon$	$\alpha'_{\text{A}}$	$\alpha'_{\text{B}}$	OH	11, 12	10, 13	others	
jojoba/formaldehyde (monoadduct) (33)											
2.11	5.10	5.50	1.99 <sup>a</sup>	-	3.30	3.48	1.66	5.31	1.99	H(A) 4.02, t, 6.7	CH <sub>2</sub> env.
m	dd	dt	m		dd	dd	br s	m	m	H(B&3) 1.58,	1.13-1.24
	15.3, 8.8	15.3, 6.7			10.4, 8.5	10.4, 5.1				quin, 7.0	$\omega$ -H, 0.85, t, 6.8
										H(2) 2.25, t, 7.5	
jojobaformaldehyde (diadduct) (DHMJ) (34)											
2.11	5.10	5.50	2.00	-	3.30	3.48	1.78	c	c	H(A) 4.02, t, 6.7	CH <sub>2</sub> env.
m	dd	dt	q		dd	dd	br s			H(B&3) 1.58,	1.14-1.39
	15.3, 8.9	15.3, 6.7	6.8		10.4, 8.5	10.4, 5.1				quin, 6.8	$\omega$ -H, 0.85, t, 6.7
										H(2) 2.25, t, 7.6	

a: overlapping with residual *cis*-allylic signals (10-H and 13-H); b: within CH<sub>2</sub> envelope; c: *cis*-unsaturation removed by ene reaction

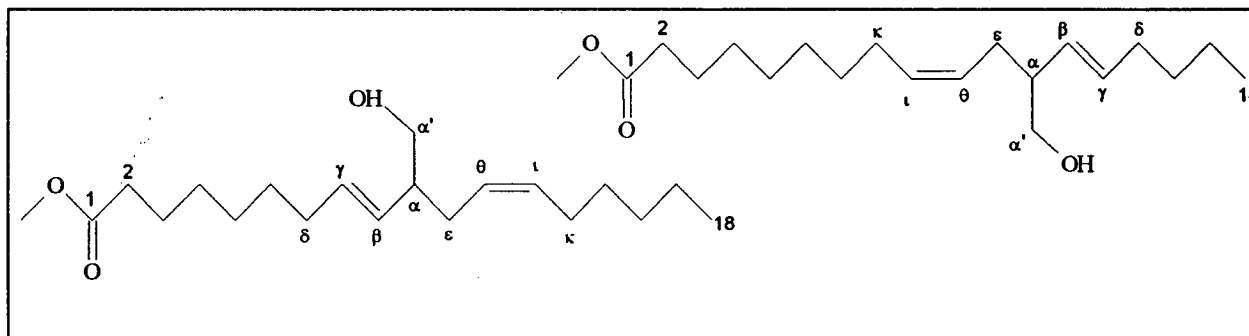
## Appendix 14



$\delta_C$ /ppm (90 MHz & 50 MHz)										
$\alpha$	$\beta$	$\gamma$	$\delta$	$\epsilon$	$\alpha'$	OH	11, 12	10, 13	others	
jojoba/formaldehyde (monoadduct) (33)										
45.73	131.13	133.65	32.48	30.95	65.81	-	129.69	26.90	C(1) 173.74	CH <sub>2</sub> env.
									C(2) 34.18	28.96-29.50
									C(3) 24.82	C( $\omega$ ) 13.90
									C(A) 64.18	C( $\omega$ -1) 22.48
									C(B) 28.47	C( $\omega$ -2) 31.71
									C(C) 25.75	
jojoba/formaldehyde (diadduct) (DHMJ) (34)										
45.79	131.12	133.85	32.52	30.97	65.82	-	a	a	C(1) 173.87	CH <sub>2</sub> env.
									C(2) 34.23	28.98-29.51
									C(3) 24.85	C( $\omega$ ) 13.96
									C(A) 64.25	C( $\omega$ -1) 22.51
									C(B) 28.49	C( $\omega$ -2) 31.72
									C(C) 25.77	

a: *cis*-unsaturation removed by ene reaction

## Appendix 15



methyl linoleate /formaldehyde (63A & B)													
$\alpha$	$\beta$	$\gamma$	$\delta$	$\epsilon$	$\theta$	$\iota$	$\kappa$	$\alpha'_A$	$\alpha'_B$	OH	18	OMe	others
$\delta_H$ /ppm, m, J/Hz (600 MHz, CDCl <sub>3</sub> and d <sub>6</sub> -benzene)													
2.20	5.19	5.51	1.99	2.13	5.32	5.39	b	3.372	3.548	c	0.870	3.65	H(2) 2.28, t,
m	ddt	5.54	2.02	m	m	5.40		3.375	3.550		0.874	s	7.5, CH <sub>2</sub> env.
	15.3,	2x dtd	2x q			2x dtt		2x dd	2x dd		2x t		1.14-1.38
	8.4, 1.5	15.3,	7.3			10.9,		10.5,	10.5,				H(3) 1.60,
		7.9, 0.9				7.1, 1.5		7.9	5.2				quin, 7.5
$\delta_C$ /ppm (50 MHz)													
45.54	130.46	132.99	32.13	?	126.72	130.83	27.05	65.36	-	13.69	51.18	C(1) 174.08	C(17) 21.94,
	130.67	133.21	32.32		126.84	130.99				13.82		C(2) 33.80	22.33
												C(3) 24.65	CH <sub>2</sub> env.
												C(16) 31.38	28.45-29.27
													27.43

a: one quartet is from  $\kappa$ -H; b: see  $\delta$ -H; c: concealed by 3-H

## Appendix 16

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